UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE NEW ENGLAND COMPOUNDING PHARMACY, INC. PRODUCTS LIABILITY LITIGATION	)	**MDL No. 2419**
	)	**Dkt. No. 1:13-md-2419 (RWZ)**
THIS DOCUMENT RELATES TO:	)	
All Cases Against The Saint Thomas Defendants	)	

PLAINTIFFS' STEERING COMMITTEE'S STATEMENT OF UNDISPUTED MATERIAL FACTS IN RELATION TO ITS MOTION FOR PARTIAL SUMMARY JUDGMENT REGARDING COMPARATIVE FAULT DEFENSES ATTRIBUTING FAULT TO GOVERNMENTAL ENTITIES

The Plaintiffs' Steering Committee, pursuant to Rule 56 of the Federal Rules of Civil Procedure and LR, D. Mass. 56.1, respectfully submits this Statement of Undisputed Material Facts in relation to its contemporaneously filed Motion for Partial Summary Judgment Regarding Comparative Fault Defenses Attributing Fault to Governmental Entities.

1. The Saint Thomas Defendants[1] assert the affirmative defense of comparative fault against the FDA, the Mass. BoP, the Tenn. BoP, and the TDH.[2]

Response:

2. The Saint Thomas Defendants assert that the FDA owed a duty to the Plaintiffs as well as their health care providers to ensure that MPA manufactured, sold, and distributed by

[1] Saint Thomas Outpatient Neurosurgical Center, LLC, Howell Allen Clinic, a professional corporation, John W. Culclasure, M.D., Debra Shamberg, R.N., St. Thomas West Hospital, formerly known as St. Thomas Hospital, Saint Thomas Network and St. Thomas Health (collectively referred to hereinafter as "the Saint Thomas Healthcare Defendants").

[2] Dkt. No. 1455 - Answer of Saint Thomas Outpatient Neurosurgical Center, LLC, Howell Allen Clinic, A Professional Corporation, John W. Culclasure, MD, and Debra V. Schamberg, RN, pg. 79, 87-90, 98-102 at ¶¶ 36, 38, 49, 54-56, 67, 69, 72-73, 76-77, 82; Dkt. No. 1464 – Saint Thomas Entities Master Answer and Affirmative Defenses to Plaintiffs' Amended Master Complaint, pg. 101, 108, 114-15, 116-17 at ¶¶ 249, 271, 286, 289, 292-94, 299).

NECC was sterile and safe for its intended use pursuant to the Federal Food, Drug, and Cosmetic Act, codified at 21 U.S.C. § 301, et seq.[3]

Response:

3. The Saint Thomas Defendants assert comparative fault against the FDA for proximately causing the alleged injuries and damages by negligently or recklessly failing to take action against NECC even though the FDA had authority to do so…[4]

Response:

4. The Saint Thomas Defendants allege that [The Mass. BoP] owed a duty to the Plaintiffs as well as their health care providers to ensure that NECC compounded medication free from contamination and operated in compliance with applicable Massachusetts pharmaceutical laws pursuant to Mass. Gen. Laws ch. 112, § 32.[5]

Response:

5. The Saint Thomas Defendants allege that the Mass. BoP proximately caused the alleged injuries and damages by negligently or recklessly failing to discipline or take action against NECC after becoming aware of NECC's failure to comply with applicable state and federal laws and manufacturing guidelines…[6]

Response:

[3] Dkt. No. 1455 at pg. 79, ¶ 36; Dkt. No. 1464 at pg. 101, ¶ 250.
[4] Dkt. No. 1455 at pg. 79, ¶ 38; Dkt. No. 1464 at pg. 101, ¶ 252.
[5] Dkt. No. 1455 at pg. 90, ¶ 56; Dkt. No. 1464 at pg. 108, ¶ 272.
[6] Dkt. No. 1455 at. pg. 92-98, ¶ 66; Dkt. No. 1464 at pg. 109-113, ¶ 279.

6. The Saint Thomas Defendants allege that [The TBoP] had the legal authority to inspect NECC, which was doing business in Tennessee as a licensee of the Tenn. BoP.[7]

Response:

7. The Saint Thomas Defendants allege that if it is established that the Tenn. BoP breached its duty by failing to timely investigate and bring charges against NECC for the violations outlined herein, failing to inquire of the Mass. BoP regarding actions against NECC, or failing to inspect NECC's facility, the Defendants assert fault against the Tenn. BoP.[8]

Response:

8. The Saint Thomas Defendants allege that the Defendants promptly complied with all instructions from the Tenn. DoH and CDC regarding contacting patients, including an initial directive from the Tenn. DoH not to mention meningitis.[9]

Response:

9. The Saint Thomas Defendants allege that the Defendants relied upon and promptly complied with all directives and guidance received from the Tenn. DoH related to this fungal meningitis outbreak.[10]

Response:

[7] Dkt. No. 1455 at pg. 100, ¶ 72; Dkt. No. 1464 at pg. 115, ¶ 288.
[8] Dkt. No. 1455 at pg. 100, ¶ 74; Dkt. No. 1464 at pg. 115, ¶ 290.
[9] Dkt. No. 1455 at pg. 101, ¶ 80; Dkt. No. 1464 at pg. 116, ¶ 297.
[10] Dkt. No. 1455 at pg. 102, ¶ 81; Dkt. No. 1464 at pg. 117, ¶ 298.

10. The Saint Thomas Defendants allege that if it is established that the Tenn. DoH did not recommend appropriate notification of patients, the Defendants are constrained to assert comparative fault against the Tenn. DoH.[11]

Response:

11. St. Thomas Neurosurgical's expert, Sheldon Bradshaw, Esq., provides the following opinion on the FDA's role in the catastrophe: "[I]F FDA had exercised its enforcement authority over NECC…the fungal meningitis outbreak of 2012 would not have occurred."[12]

Response:

12. St. Thomas Neurosurgical's expert, Dr. Henry Miller, provides the following opinion on the FDA and the MBoP's role in the catastrophe: "[T]he FDA and [MBoP] failed to exercise proper regulatory authority over NECC and failed to take the objectively reasonable regulatory actions that would have prevented the fungal meningitis outbreak of 2012. The FDA and the [MBoP] are both at fault…"[13]

Response:

13. No Defendant has offered any expert proof regarding TBoP or TDoH's actions or inactions causing any of plaintiffs' injury.[14]

Response:

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[11] Dkt. No. 1455 at pg. 102, ¶ 82; Dkt. No. 1464 at pg. 117, ¶ 299.
[12] Expert Report of Sheldon Bradshaw, Esq., pg. 30.
[13] Expert Report of Dr. Henry Miller, pg. 29.
[14] *See generally* Expert Report of Sheldon Bradshaw, Esq. (attached hereto as "Exhibit 1" and incorporated by reference herein) and Expert Report of Dr. Henry Miller (attached hereto as "Exhibit 2" and incorporated by reference herein).

Date: May 9, 2016

Respectfully Submitted:

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CERTIFICATE OF SERVICE

I, Benjamin A. Gastel, hereby certify that I caused a copy of the foregoing to be filed electronically via the Court's electronic filing system. Those attorneys who are registered with the Court's electronic filing system may access these filings through the Court's system, and notice of these filings will be sent to these parties by operation of the Court's electronic filing system.

Date: May 9, 2016

/s/ J. Gerard Stranch, IV
J. Gerard Stranch, IV

EXHIBIT "A"

SHELDON BRADSHAW, ESQ.

SHELDON T. BRADSHAW, ESQ.

I, Sheldon T. Bradshaw, hereby declare as follows:

1. I have been retained by the law firm of Gideon, Cooper & Essary ("Gideon") to provide expert opinion testimony on the U.S. Food and Drug Administration ("FDA") and FDA regulatory matters. In particular, Gideon has asked me to provide expert opinion testimony on FDA's regulation of pharmacy compounding.[1]

I. Background and Statement of Qualifications

2. I am a partner in the international law firm of Hunton & Williams LLP ("Hunton & Williams"), where I co-chair the firm's Food and Drug Practice Group. At Hunton & Williams I represent food, drug, biologic, medical device, cosmetic, and dietary supplement manufacturers on the full range of issues confronting FDA-regulated firms. I have also represented clients that own and operate pharmacies.

3. My practice includes providing advice on FDA regulatory matters; assisting companies in FDA enforcement matters; FDA compliance counseling; helping firms respond to FDA investigations and inquiries, including those alleging labeling violations; conducting litigation; carrying out legislative initiatives; performing due diligence and other transactional work; and advising clients on the practices of medicine and pharmacy.

[1] I understand that Gideon represents Saint Thomas Outpatient Neurosurgical Center, LLC ("STOPNC"), and its affiliated entities, Howell Allen Clinic,("Howell Allen"), John W. Culclasure, MD ("Dr. Culclasure"), Debra Schamberg, RN, CNOR ("Ms. Schamberg"); and Vaughan Allen, MD.("Dr. Allen"); and Specialty Surgery Center, PLLC ("SSC") and its affiliated entities, Kenneth R. Lister, MD, P.C. ("Dr. Lister"). I refer to Gideon's clients collectively as "Defendants."

4. In the course of my practice I have advised numerous clients on issues related to FDA's authority to regulate pharmacy compounding and have served as an expert witness on the same subject.[2] I have also written articles on the Agency's authority to regulate pharmacy compounding[3] and have been interviewed by numerous news organizations on the subject.[4]

5. Prior to joining Hunton & Williams in October of 2007, I was the Chief Counsel of the FDA. As Chief Counsel, I was responsible for overseeing an office of approximately 80 attorneys and for providing legal advice to the Secretary and Deputy Secretary of the U.S. Department of Health and Human Services and to FDA's senior leadership -- including the Commissioner, the Deputy Commissioners, and the Directors of the various FDA Centers. I provided advice on legal issues related to drugs, biologics, cosmetics, medical devices, food, animal feed and drugs, dietary supplements, and other products regulated under the Federal Food, Drug, and Cosmetic Act ("FD&C Act") and the Public Health Service Act.

6. As Chief Counsel, I oversaw the Agency's litigation docket, which included cases involving FDA's authority to regulate compounded drugs and compounding

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[2] *See United States of America v. Franck's Lab, Inc.*, Civil Action No. 5:10-cv-00147-TJC-GRJ (U.S. D.Ct., M.D. Florida).

[3] Co-author, *FDA Watch, New Compounding Legislation*, *Contract Pharma* (Jan. 24, 2014); Co-author, *A Compounding Fracture at the FDA*, *Wall Street Journal* (Nov. 13, 2012); Co-author, *Did FDA Apply a Remedy Worse than the Disease in Refusing to Clear the Market of Unapproved Versions of Makena?* *FDLI's Food and Drug Policy Forum*, Volume 1, Issue 11 (June 2011).

[4] *See CBS Evening News* (Oct. 19, 2012); For Your Ears Only - Message of Meningitis, *Newsweek Radio* (Oct. 14, 2012); *FDA Regulation Of Pharmacies Has Knotty History*, *The Associated Press* (Oct. 12, 2012); *Explaining Compound Drugs and Their Ties to Fungal Meningitis Outbreak*, *Philly.com* (Oct. 11, 2012); *Meningitis Outbreak: FDA Had Chance But Didn't Stop Compounding Pharmacy*, *The Tennessean* (Oct. 10, 2012); *Critics: Obama Shares Outbreak Blame*, *Boston Herald* (Oct. 10, 2012); *Meningitis Outbreak Reveals Regulatory 'Black Hole'*, *Radio Boston (WBUR)* (Oct. 9, 2012); *Oversight Eyed in Outbreak*, *Boston Herald* (Oct. 8, 2012); *NBC Nightly News with Brian Williams* (Oct. 8, 2012); *ABC World News Tonight* (Oct. 7, 2012); *CBS News Radio* (Oct. 7, 2012); *Scant Oversight of Drug Maker in Fatal Meningitis Outbreak*, *The New York Times* (Oct. 6, 2012).

pharmacies. I also personally reviewed and cleared every Warning Letter issued by the FDA, many of which discussed FDA's authority to regulate pharmacy drug compounding. I also spoke with the recipients of such Warning Letters and, because I oversaw all FDA-related litigation, was significantly involved in determining whether their noncompliance would result in FDA bringing an enforcement action.

7. In addition, I regularly advised the senior leaders of FDA's Center for Drug Evaluation and Research ("CDER"), which is responsible for regulating human drugs, and FDA's Center for Veterinary Medicine ("CVM"), which is responsible for regulating animal drugs, on matters related to pharmacy compounding in general and the distinction between traditional pharmacy compounding and manufacturing (under the guise of pharmacy compounding) in particular. I also routinely advised senior leaders of FDA's Office of Regulatory Affairs ("ORA"), which is responsible for overseeing FDA field operations, and others within the FDA, including the FDA Commissioner, on the same subjects.

8. Prior to joining FDA in March of 2005, I held several senior positions at the U.S. Department of Justice ("DOJ"), including the position of Deputy Assistant Attorney General in DOJ's Office of Legal Counsel ("OLC"). OLC provides authoritative legal advice on statutory and constitutional questions from the President and all of the Executive Branch agencies.[5] While at OLC I provided legal advice to the Chief Counsel of the FDA and twice testified before the U.S. Senate on legislation amending the FD&C Act.

[5] *See* http://www.justice.gov/olc/.

9. My *curriculum vitae* is attached as Exhibit 1. All of the publications I have authored over the previous ten (10) years are listed on my *curriculum vitae.*

10. I am being compensated at the rate of $800 per hour for the time I have spent on this matter. I will also be reimbursed for all expenses associated with this engagement. My compensation is not in any way dependent on the opinions set forth in this declaration or on the outcome of the litigation.

11. Set forth below is a list of all other cases in which I have testified as an expert at trial or by deposition in the last four (4) years. The name of the party for which I testified is identified in **bold**.

a) **Apotex Holdings Inc. and Apotex Inc.** v. The Government of the United States of America. ICSID Case No. ARB(AF)/12/1. NAFTA Tribunal in Washington DC.

b) ***Athena Cosmetics, Inc., Pharma Tech International, Inc. and Northwest Cosmetic Laboratories, LLC*** *v. Allergan. Case No. SACV07-1316 JVS (RNBx).* C.D. Cal. *Consolidated with Case No. SACV09-0328 JVS (RNBx).* C.D. Cal.

c) **Nautilus Neurosciences, Inc. and APR Applied Pharma Research SA v.** Wockhardt USA LLC, and Wockhardt LTD. *Civil Action No. 2:11-1997 (ES/CL).* D.N.J.

d) SANDOZ INC., a New Jersey corporation vs. **AMGEN INC.**, a Delaware corporation and **HOFFMANN-LA ROCHE INC.**, a New Jersey corporation. *Case No. 3:13-cv-02904-MMC.* N.D. Cal.

e) **[Redacted]** vs. [Redacted]. *ICC Case No. 19074/CYK.* Confidential arbitration between private parties in Singapore.

f) *Ex rel.* Beverly Brown vs. **Celgene Corporation**, Case No. 10-cv-03165 GHK (SSx). C.D. Cal.

II. Information Relied Upon

12. In forming my opinions, I relied on my education, training, experience, and the materials I reviewed, including the following:

a) Massachusetts Board of Pharmacy regulatory documents concerning NECC contained in the attached CD.

b) FDA regulatory documents concerning NECC contained in the attached CD.

c) The PSC's (hereinafter "Plaintiffs") Second Amended Master Complaint.

d) The Complaint from the *Reed* case.

e) The Complaint from the *Bumgarner* case.

f) STOPNC, *et al.*'s Master Answer.

g) April 16, 2013 House of Representatives Staff Report: "FDA's Oversight of NECC and Ameridose: A History of Missed Opportunities?"

h) Transcript of the Deposition of Samuel Penta testifying as the Massachusetts Board of Pharmacy.

i) David A. Kessler, MD's Rule 26 Disclosure.

j) Gregory A. Conigliaro's Memorandum of Law in Support of His Motion To Dismiss Count 3 of the Indictment.

k) Additional materials specifically referenced or cited to in the text of my report.

III. Summary of Conclusions

13. Administering and prescribing drugs compounded by pharmacies has historically been a core component of the practice of medicine in the United States. Even with the ever increasing number of FDA-approved drug products that are commercially available, the FDA recognizes the important public health function served by compounding pharmacies as there are still a number of therapeutically important drug products that health care practitioners can only obtain from compounding pharmacies.

14. While the Agency recognizes a distinction between traditional pharmacy compounding and drug manufacturing (performed under the guise of traditional pharmacy compounding), FDA has for several decades consistently taken the position (in Compliance Policy Guides, in Warning and Untitled Letters, and in litigation) that all compounded drugs are "new drugs" under the FD&C Act and that the Agency, therefore, possesses the necessary authority under the FD&C Act to regulate all pharmacy compounding. The FDA states, however, that it normally exercises enforcement discretion with regard to traditional pharmacy compounding, and instead focuses on actively regulating pharmacy compounding that is more akin to drug manufacturing.

15. It is obvious from the documents that I reviewed that the New England Compounding Center ("NECC") was operating more like a drug manufacturer. As a result, not only was NECC subject to FDA's regulatory authority, they were the very type of facility that FDA had repeatedly stated it was directing its enforcement resources against. Despite the Plaintiffs' suggestion to the contrary, there can be no

doubt, in light of FDA's repeated statements on this point, that FDA considered NECC to be an FDA regulated entity. If that was not clear from the 2006 Warning Letter that FDA issued to NECC, it should have been perfectly clear to anyone who read the 2008 letter that FDA sent to NECC in which the Agency forcefully reasserted its jurisdiction over NECC.

16. The first time I ever heard FDA state that its legal authority over pharmacy compounding was inadequate or unclear was in response to stinging criticism the Agency received in 2012 for its abject failure to take any action against NECC prior to the deadly outbreak of fungal meningitis. In light of FDA's prior (and repeated) statements regarding its legal authority to regulate compounding pharmacies like NECC (or, more pointedly, in light of FDA's prior statements regarding its authority to regulate NECC), FDA's claims of inadequacy are clearly a post hoc rationalization meant to justify its inaction and to deflect unwanted criticism. Indeed, a subsequent congressional investigation likewise concluded that the Agency (consistent with its prior statements regarding its authority over pharmacy compounding) had ample authority to take enforcement action against NECC in the months and years preceding the fungal meningitis outbreak.

17. In a complaint filed against a compounding pharmacy on January 4, 2016, the government (on FDA's behalf) took the position that prior to the enactment of Section 503B of the FD&C Act in 2013, all pharmacy compounding had to comply with the conditions set forth in Section 503A of the FD&C Act, which included, among other conditions, that compounded drugs must be prepared pursuant to patient-specific prescriptions. In the complaint the Agency also took the position that both before and

after the enactment of Section 503B of the FD&C Act, drugs are deemed to be adulterated under Section 501(a) of the FD&C Act if they are compounded under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health. Based on those positions, FDA should have taken an enforcement action against NECC well before the fungal meningitis outbreak.

18. FDA has long stated that the Agency has the authority to take enforcement actions against a compounding pharmacy operating in violation of the FD&C Act, including moving to permanently restrain and enjoin the compounding pharmacy from compounding, packaging, holding or distributing any drugs. FDA also has the ability to issue a "Safety Alert" to healthcare practitioners when it believes sterile drug products were compounded under insanitary conditions or are contaminated.

19. Following the Agency's 2006 issuance of a Warning Letter to NECC, FDA was aware that NECC was still compounding sterile injectable drugs under insanitary conditions, but nevertheless failed to take any action to enjoin NECC's compounding operations or to alert healthcare practitioners regarding the Agency's concerns. At a minimum, FDA should have issued a Safety Alert to healthcare practitioners. And, when it became clear that NECC had not taken (or would not take) the necessary remedial action requested by FDA, the Agency should have taken steps to enjoin NECC's operations. Likewise, the Massachusetts Board of Pharmacy ("MBP") should have taken more aggressive action against NECC.

20. Plaintiffs have suggested that NECC's failure to require patient specific prescriptions prior to distributing methylprednisolone acetate ("MPA") should have

been a red flag to Defendants. As noted above, NECC was operating as a drug manufacturer (and drug manufacturers do not require prescriptions), and there was no reason for healthcare practitioners to have thought they were anything but a manufacturer.[6] In any event, since FDA was fully aware of NECC's practice of distributing drugs without a prescription and took no steps to prevent it (although it had asserted the power to do so), it is not clear to me why healthcare practitioners should have been expected to second guess the Agency. Healthcare practitioners – who are simply not in a position to investigate every single manufacturer from whom they source drugs – rightfully rely on FDA, the world's premier authority on drug safety, to ensure that entities under their jurisdiction (such as compounding pharmacies operating as drug manufacturers) are complying with the FD&C Act.

21. In light of FDA's failure to take any public enforcement action against NECC following the Warning Letter in 2006 or to issue a Safety Alert, there was no reason for healthcare practitioners in 2011 to believe that they should not be sourcing sterile injectable drugs from NECC, which was transparently manufacturing and distributing sterile injectable drugs without prescriptions with FDA's knowledge and under FDA's watch. I would further observe that even if NECC had obtained prescriptions from Defendants prior to distributing drugs to them, doing so would not have prevented the fungal meningitis outbreak caused by NECC compounding and distributing contaminated drugs.

[6] Based on my own experience, a healthcare practitioner in 2011 would not have known (or have been expected to know) the difference between traditional pharmacy compounding on one hand and pharmacy compounding more closely associated with drug manufacturing on the other. Based on their practices, it is my opinion that in 2011 a healthcare practitioner would have no reason to believe that NECC was anything other than drug manufacturer.

22. Plaintiffs have also suggested that Defendants had a duty to contact FDA, ostensibly through the Freedom of Information Act ("FOIA"), to request information regarding the manufacturers of drugs that they administered or prescribed. While I cannot speak to whether or not any such duty exists or, if so, the source of such a duty, based on my experience at FDA I can state that healthcare practitioners do not regularly or routinely submit FOIA requests to FDA for such information. I can also state that the Agency would not want to encourage such a practice as FDA would quickly become overwhelmed if every healthcare practitioner in the United States made such a submission. Indeed, FDA would do nothing but respond to FOIA requests if such a practice were common. I would further observe that had Defendants submitted a FOIA request in 2011 for information concerning NECC, they would likely have received (after waiting for months) little more than the 2006 Warning Letter as internal agency deliberations regarding NECC would have been treated as exempt from disclosure. As explained in the preceding paragraph, obtaining the 2006 Warning Letter in 2011 would not have shed any light on NECC's current status in light of FDA's inaction.

IV. Pharmacy Compounding

23. As explained in greater detail below, administering and prescribing drugs compounded by pharmacies has historically been a core component of the practice of medicine in the United States. Indeed, FDA has long recognized the important public health function served by traditional pharmacy compounding.

24. Pharmacy compounding—which the Supreme Court has described as the "process by which a pharmacist or doctor combines, mixes, or alters ingredients to

create a medication tailored to the needs of an individual patient,"[7]—has historically been a core component of the practice of pharmacy in the United States. In fact, drug compounding was performed by some of the very first colonists. For example, in the 17th century, John Winthrop, Jr., the son of the first governor of Massachusetts, engaged in pharmacy drug compounding.[8] The United States Pharmacopoeia ("USP"), an official compendium of drug information recognized as authoritative by the FD&C Act,[9] has included instructions on compounding since 1820.[10]

25. The FD&C Act was enacted in 1938 against the backdrop of widespread traditional pharmacy compounding conducted under State law and regulation. At that time, traditional pharmacy compounding was widely practiced, as it was often the only way to supply healthcare practitioners with the drugs they needed to treat their patients. In fact, with only a few (though steadily increasing number of) drug companies commercializing their drug products, pharmacists compounded more than 250 million prescriptions per year prior to 1938.[11] Of particular importance, every State's pharmacy law defined the practice of pharmacy to include drug compounding for physicians and their patients.[12]

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[7] *See Thompson v. Western States Med. Ctr.*, 535 U.S. 357, 360-61 (2002).
[8] *See Remington's Practice of Pharmacy* 13 (12th ed. 1961).
[9] *See* FD&C Act § 201(j).
[10] *See* Claudia C. Okeke, et al., *History and Background Information on USP's Activities in Compounding Pharmacy Practices*, 27 Pharmacopeial Forum 3169, 3169 (Sep.-Oct. 2001).
[11] *See Proceedings of the Local Branches*, 14 J. Am. Pharm. Ass'n 232, 233 (1935).
[12] *See Joint Session of the American Pharmaceutical Association, the American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy*, 17 J. Am. Pharm. Ass'n 1000, 1010-13 (1938).

26. When enacted in 1938, the FD&C Act did not specifically address pharmacy drug compounding. Instead, FDA was broadly given the authority to regulate new drugs. Initially, FDA's focus was on companies that were commercializing their new drug products and the historic practice of traditional pharmacy compounding was regulated under State law. Over the course of the next several decades, the number of compounded drugs decreased as the number of FDA-approved drugs increased.

27. In the late 1980s and early 1990s, however, FDA became increasingly aware of (and troubled by) the emergence of large compounding facilities that, while licensed as pharmacies and run by licensed pharmacists, were not in fact making unique medications for identified individual patients pursuant to valid prescriptions from licensed prescribers, but instead were making and distributing in large quantities what often were simply copies of FDA-approved drugs that were commercially available. These facilities typically marketed their products, which they often gave unique trade names, directly to doctors through their own sales forces. The Agency was concerned that, under the guise of traditional pharmacy compounding, these facilities were engaged in the type of drug manufacturing and distribution that FDA regularly regulated under the FD&C Act.

28. In light of the Agency's newfound concerns, FDA published a Compliance Policy Guide ("CPG") in 1992 that offered guidance to pharmacies compounding drugs for human use.[13] Following the issuance of the CPG, FDA took a series of enforcement actions under the FD&C Act against compounding pharmacies that the Agency believed were engaged in drug manufacturing (albeit under the guise of

[13] *See* CPG 7132.16 (Mar. 1992) (later renumbered as CPG 460.200).

traditional pharmacy compounding). In response to FDA's actions, pharmacists sought clarification from Congress regarding FDA's authority to regulate the practice of pharmacy. In 1997, Congress responded by enacting Section 127 of the Food and Drug Administration Modernization Act ("FDAMA"), which is codified as Section 503A of the FD&C Act.

29. Section 503A of the FD&C Act authorizes pharmacists to compound drugs without having to comply with three requirements of the FD&C Act (i.e., the new drug approval requirement in Section 505(a), the current good manufacturing practices ("cGMP") requirement in Section 501(a)(2)(B), and the adequate-directions-for-use labeling requirement in Section 502(f)(1)), so long as certain conditions are complied with. For example, compounding must (1) be performed by a licensed pharmacist in a licensed facility and (2) be pursuant to a valid prescription for an identified individual patient made by a licensed practitioner.[14] While a compounding pharmacy need not comply with FDA's strict cGMP requirements, Section 503A did not exempt pharmacies from the general prohibition against compounding drugs under insanitary conditions in Section 501(a)(2)(A) of the FD&C Act.

30. In addition, under Section 503A pharmacists may compound limited quantities of drugs in anticipation of receiving a valid prescription based on a history of the pharmacist receiving valid prescription orders for the compounding of the drug product,[15] and they may compound from bulk ingredients.[16] While pharmacists may not compound "regularly or in inordinate amounts . . . any drug products that are

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[14] *See* FD&C Act § 503A(a).
[15] *See id.* § 503A(a)(2)(A)-(B).
[16] *See id.* § 503A(b)(1)(A).

essentially copies of a commercially available drug product,"[17] Congress made it crystal clear that a compounded drug was not "essentially a copy of a commercially available drug product" if the difference "between the compounded drug and the comparable commercially available drug product" is significant for the patient "as determined by the prescribing practitioner."[18] These requirements are consistent with the well-established definition of traditional pharmacy compounding.

31. FDA's initial attempt to enforce Section 503A was shelved in 2002, however, shortly after the Supreme Court found the advertising, promotion, and solicitation provisions in Section 503A to be unconstitutional in *Thompson v. Western States Medical Center.*[19] Although the Supreme Court found the advertising, promotion, and solicitation provisions in Section 503A to be unconstitutional, it did not address whether those provisions could be severed from Section 503A, leaving the remaining provisions intact and enforceable. FDA took the position that the unconstitutional provisions were integral to Section 503A and, therefore, were not severable. As a result, the Agency determined that Section 503A was inoperative and, in May 2002, the Agency reverted to regulating pharmacy compounding via a CPG, as it did prior to the 1997 enactment of Section 503A.[20]

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[17] *See id.* § 503A(b)(1)(D).

[18] *See id.* § 503A(b)(2) (emphasis added). It is my understanding that SSC utilized compounded MPA because it was preservative free, and they had concerns, based on reports published in peer reviewed journals, about complications related to preservatives contained in the FDA-approved MPA that was commercially available. Because the patient need for the preservative free formulation of MPA was determined by the prescribing practitioner, it is my opinion that the compounded drug would not be considered to be essentially a copy of the commercially available drug product.

[19] *See* 535 U.S. 357 (2002).

[20] *See* FDA, CPG 460.200, *Pharmacy Compounding* (May 2002), *withdrawn* 78 Fed. Reg. 72,901 (Dec. 4, 2013).

32. As was the case prior to 1997, FDA noticed that a number of large compounding facilities appeared to be compounding under insanitary conditions. In addition, many of these compounding facilities were not in fact compounding unique medications for identified individual patients pursuant to valid prescriptions from licensed prescribers—a practice not permitted under either the CPG or Section 503A. One such facility was NECC, which received a Warning Letter from FDA regarding its compounding practices in December of 2006.[21]

33. After FDA issued the Warning Letter to NECC, the U.S. Court of Appeals for the Fifth Circuit ruled that the provisions in Section 503A that the Supreme Court found to be unconstitutional in the *Western States* case were in fact severable and that Section 503A (sans the unconstitutional provisions) still governed the practice of traditional pharmacy compounding.[22] Now, in addition to the statutory authorities cited in the CPG, FDA once again had Section 503A of the FD&C Act at its disposal. Despite those authorities, and FDA's statements to NECC that the Agency had the legal authority to regulate its activities, FDA took no additional action against NECC even though the Agency had reason to believe that NECC was still compounding sterile injectable drugs under insanitary conditions.

34. In 2012, steroid injections compounded by NECC caused an outbreak of fungal meningitis in the United States. The steroids, which were compounded under insanitary conditions, were injected into the spines of thousands of patients.

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[21] *See* Letter from Gail Costello, District Director, New England District Office, FDA, to Barry J. Cadden, Director of Pharmacy and Owner, New England Compounding Center (Dec. 4, 2006), *available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076196.htm.

[22] *See* Med. Ctr. Pharmacy v. Mukasey, 536 F.3d 383 (5th Cir. 2008).

Ultimately, 64 people died and hundreds more were treated for persistent fungal infections.

35. In direct response to the deadly outbreak of fungal meningitis caused by NECC, Congress enacted the Compounding Quality Act on November 27, 2013. The Compounding Quality Act amended Section 503A by removing the advertising provisions found to be unconstitutional by the Supreme Court in *Western States*, and adding Section 503B to the FD&C Act. Congress's clear purpose was to continue to regulate traditional pharmacy compounding under existing Section 503A and to regulate compounding facilities *not* engaged in patient-specific dispensing (that, therefore, cannot lawfully engage in compounding under Section 503A), i.e., facilities like NECC, as outsourcing facilities under the new Section 503B.

36. Under Section 503B, a facility at one geographic location or address that is engaged in the compounding of sterile drugs may elect to register as an outsourcing facility (though, of note, if a facility cannot comply with the requirements set forth in Section 503A, "electing" to register as an outsourcing facility is the only option for such a facility if it wants to lawfully compound drug products). An outsourcing facility may compound drugs without obtaining valid prescriptions from licensed prescribers for identified individual patients, but to do so the facility must comply with *all* of the requirements of Section 503B. Among other things, Section 503B requires that outsourcing facilities provide certain information to FDA about the products they compound, submit adverse event reports to the Agency, and comply with cGMP requirements under Section 501(a)(2)(B) of the Act.

37. Regulations that FDA has promulgated pursuant to Section 501(a)(2)(B) regarding cGMP requirements for the manufacture of drug products are set forth in 21 C.F.R. parts 210 and 211. While FDA intends to promulgate more specific cGMP regulations for outsourcing facilities, the Agency has issued a draft guidance entitled *Current Good Manufacturing Practice—Interim Guidance for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act.*[23] FDA issued the draft guidance as "interim guidance," explaining that the document describes FDA's expectations regarding outsourcing facilities' compliance with the cGMP requirements in 21 C.F.R. parts 210 and 211 until more specific cGMP regulations for outsourcing facilities are promulgated.

38. In the interim guidance, FDA stated that it expects 503B outsourcing facilities to comply with cGMP regulations dealing with: (1) facility design; (2) control systems; (3) environmental and personnel monitoring; (4) equipment, containers, and closures; (5) components; (6) production and process controls; (7) release testing; (8) laboratory controls; (9) stability/expiration dating; (10) packaging and labels; and (11) complaint handling.[24]

V. FDA's Authority to Regulate Pharmacy Compounding

39. The Agency has for decades taken the position (in Compliance Policy Guides, in Warning and Untitled Letters, and in litigation) that it has all the authority necessary under the FD&C Act to regulate the practice of pharmacy compounding.

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[23] *See* FDA, Draft Guidance for Industry, *Current Good Manufacturing Practice—Interim Guidance for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act* (July 2014).

[24] *See id.* at § III.

A. FDA Statements in Compliance Policy Guides

40. To address its concerns regarding establishments with pharmacy licenses manufacturing unapproved new drugs under the guise of traditional pharmacy compounding, FDA issued CPG 7132.16 on March 16, 1992. CPG 7132.16 stated FDA's longstanding policy of deferring to state regulation of pharmacies engaged in traditional pharmacy compounding activities, but stated that FDA was issuing the CPG to identify those circumstances under which it believed establishments with retail pharmacy licenses were engaged in "manufacturing, distributing, and promoting unapproved new drugs" in a manner outside the traditional pharmacy practice of compounding.[25] The CPG specifically described traditional pharmacy compounding to consist of the compounding of "reasonable quantities of drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner."[26] According to the CPG, the Agency clearly had the enforcement authority to take action against such establishments for violations of the FD&C Act's new drug approval, adulteration, and misbranding provisions.[27]

41. After the Supreme Court's decision in *Western States*, FDA issued CPG 460.200 to provide "guidance to drug compounders and the staff of the Food and Drug Administration (FDA) on how the Agency intends to address pharmacy compounding of human drugs."[28] CPG 460.200 reasserted FDA's authority to regulate drug compounding by pharmacies under the FD&C Act and outlined the

[25] FDA, CPG 7132.16, *Manufacture, Distribution, and Promotion of Adulterated, Misbranded, or Unapproved New Drugs for Human Use by State-Licensed Pharmacies* (Mar. 16, 1992), *superseded by* Section 503A of the FD&C Act.

[26] *Id.*

[27] *See id.*

[28] FDA, CPG 460.200, *Pharmacy Compounding* (May 2002), *withdrawn* 78 Fed. Reg. 72,901 (Dec. 4, 2013).

manner in which the Agency would exercise that broad authority. Specifically, the Agency said that it would "continue to defer to state authorities regarding less significant violations of the [FD&C] Act related to pharmacy compounding of human drugs."[29] Instead, FDA stated in the CPG that it would focus its enforcement efforts on the "increasing number of establishments with retail pharmacy licenses . . . engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that [are in violation of] the Act."[30] The CPG described the firms that would be the focus of Agency action as firms that "receive and use large quantities of bulk drug substances to manufacture large quantities of unapproved drug products in advance of receiving a valid prescription for them" and "sell to physicians and patients with whom they have only a remote professional relationship."[31] For such firm, the CPG intoned, "FDA has determined that it should seriously consider enforcement action."[32] The CPG made it absolutely clear that "FDA-initiated regulatory action may include issuing a warning letter, seizure, injunction, and/or prosecution."[33]

42. In sum, during the periods when FDA announced its authority to regulate pharmacy drug compounding in accordance with CPGs, the Agency consistently and repeatedly took the position that it had ample authority under the FD&C Act to regulate—including by bringing enforcement actions—pharmacy compounding.

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[29] *Id.* at 3.
[30] *Id.*
[31] *Id.*
[32] *Id.*; *see also id.* at 3-4 (listing other factors FDA would consider when determining whether to take action).
[33] *Id.* at 4.

B. FDA Statements in Litigation

43. In both its initial brief and its reply brief in *Western States*, the government (on behalf of FDA) asserted to the U.S. Supreme Court that, prior to the enactment of Section 503A in 1997, compounded drugs were "new drugs" subject to FDA's full regulatory authority. The government's initial brief stated that as a matter of enforcement discretion the Agency historically had not brought enforcement actions against pharmacies engaged in traditional pharmacy compounding, but stated that that "FDA did take action . . . when compounding was outside the scope of normal pharmacy practice and compounded drugs were mass-produced and distributed in a manner tantamount to the manufacture of unapproved new drugs."[34]

44. Likewise, in its reply brief in *Western States*, the government specifically stated that, as "an initial matter, compounded drugs are not exempt from the new drug approval requirements"; that FDA has "long taken the position that drugs compounded by pharmacies are subject to the new drug approval requirements"; and that the enactment of Section 503A confirms this by allowing a limited exemption.[35] These claims of authority to regulate pharmacy compounding were also made in the government's earlier Ninth Circuit Brief in the same matter.[36]

45. Subsequent to the *Western States* cases, the government continued to assert that it had legal authority to regulate pharmacy compounding. In *Wedgewood Village*

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[34] Brief for the Petitioners, *Thompson v. Western States Med. Ctr.*, 2001 WL 1605836, *5-6 (U.S.).

[35] Reply Brief of Petitioners, *Thompson v. Western States Med. Ctr.*, 2002 WL 243584, *4-16 (U.S.). As noted above, the Supreme Court invalidated Section 503A's advertising provisions on First Amendment grounds. *See Thompson v. Western States Med. Ctr.*, 535 U.S. 357 (2002).

[36] *See* Brief for Appellants, *Western States Med. Ctr. v. Shalala*, 2000 WL 34004737 (9th Cir.).

Pharmacy, Inc. v. United States,[37] the government explicitly stated that it had the authority to take enforcement actions against compounding pharmacies, including inspections. In numerous other cases occurring prior to the fungal meningitis outbreak in 2012, the government asserted time and again that FDA had the authority to regulate compounding pharmacies.[38]

46. Interestingly, in a complaint for permanent injunction filed only days ago against a compounding pharmacy in Texas, the government reaffirmed that FDA had the necessary authority to regulate compounding pharmacies prior to the fungal meningitis outbreak. In *United States of America v. Downing Labs, LLC*, the government (on behalf of FDA) explicitly asserted that conduct that occurred before the enactment of Section 503B in 2013 could be the basis for an enforcement action if the conduct did not comply with the conditions set forth in Section 503A.[39] The government then gave two specific examples of conduct that justified its seeking to enjoin the compounding pharmacy's operations: (1) compounding drugs without patient-specific prescriptions,[40] and (2) compounding drugs under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health.[41] To be clear, the government (only days ago on January 4, 2016) has specifically stated that FDA had the necessary authority to enjoin a compounding pharmacy's operations in 2012 if the pharmacy was compounding drugs (1) without patient-specific prescriptions or (2) under insanitary conditions.

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[37] 2004 WL 5040342 (3rd Cir. 2004).

[38] *See, e.g.*, Briefs in Medical Center Pharmacy v. Gonzales and Medical Center Pharmacy v. Holder in 2007 and 2010, respectively.

[39] *See* Complaint for Permanent Injunction Against Downing Labs, LLC, ¶ 41, Civil Action No. _____, Filed January 4, 2016 (U.S. D.Ct. N.D. Tex.).

[40] *See id.* at ¶ 41.

[41] *See id.* at ¶ 28.

C. FDA Statements in Warning Letters

47. As in litigation, FDA has asserted in numerous Warning Letters issued during the time period preceding the fungal meningitis outbreak in 2012 that the Agency had full authority to regulate pharmacy compounding under the FD&C Act. Warning Letters to compounding pharmacies during this time stated that "FDA's position is that the . . . FDCA establishes agency jurisdiction over 'new drugs,' including compounded drugs."[42] The letters further stated that "FDA historically has not taken enforcement actions against pharmacies engaged in traditional pharmacy compounding," instead directing its enforcement resources against those companies

[42] *See, e.g.*, Warning Letter to Mr. Raul Sanchez, President, Farmacia La Salud Inc., from Maridalia Torres, District Director, San Juan District (26-Mar-08); Warning Letter to James G. Castillo, President, Tiberius Inc., from Emma R. Singleton, Director, Florida District (04-Dec-06); Warning Letter to Mr. Justin M. Kohli, Vice President, Essential Pharmacy Compounding, from John W. Thorsky, Acting District Director, Kansas City District (07-Jan-05); Warning Letter to Mr. Harold Keller, Hal's Compounding Pharmacy, Inc., from Mike M. Levy, Director, Division of New Drugs and Labeling Compliance, Office of Compliance, Center for Drug Evaluation (04-Dec-06); Warning Letter to Mr. Scott T. Popyk, Owner, Health Dimensions, Inc., from David M. Kaszubski, Acting District Director, Detroit District Office (27-Nov-06); Warning Letter to Mr. Gene Ragazzo, R.Ph, Mr. James Palmieri, R.Ph, Co-owners, Drugs Are Us, Inc. DBA Hopewell Pharmacy, from Douglas L. Ellsworth, District Director, New Jersey District, (07-Jun-04); Warning Letter to Mr. Haskell Kohen Tabor, D.Ph., President, Kalchem International, Inc., from Michael M. Levy, Director, Division of New Drugs, Labeling, and Compliance, Center for Drug Evaluation and Research (08-Jan-07); Warning Letter to Stephen R. Caudle, Owner, Line Avenue Pharmacy, from H. Tyler Thornburg, District Director, New Orleans District, (07-Jun-04); Patrick Willingham, President and CEO, Med-South Pharmacy, Inc., dba Partners In Care H. Tyler Thornburg, District Director, New Orleans District, (28-Sep-07); Warning Letter to Ms. Susan Merenstein, Owner, Murray Avenue Apothecary, from Thomas D. Gardine, District Director, Philadelphia District Office (07-Jan-08); Warning Letter to Daniel A. Newman, President, Newman Inc., dba Medi-Stat, from H. Tyler Thornburg, District Director, New Orleans District (24-Jun-08); Warning Letter to Mr. Joel Maertens, R.Ph, Owner, Palace Pharmacy, from B. Belinda Collins, District Director, 23-Mar-05; Warning Letter to Bill Swail, President, Peoples Pharmacy, Inc., from Michael A. Chappell, Director, Dallas District, 07-Jun-2004; Warning Letter to Mr. James Porter, Owner, Pharmacy Compounding Specialties, from Elaine R. Crosby, Acting Director, Dallas District, 07-Jan-08; Warning Letter to Mr. John Scott Karolchyk, R.Ph., Mr. Bernard Covalesky, R.Ph., Co-Owners, Pharmacy Creations, from Douglas I. Ellsworth, District Director, New Jersey District, 31-Oct-06; Warning Letter to Mr. David N. Jonas, Chairman/CEO, PharMEDium Services, LLC, from Michael A. Chappell, Director, Dallas District, (13-Apr-2007); Warning Letter to Mr. Thomas Reed and Ms. Dana Reed-Kane, Owners, Reed's Compounding Pharmacy, from Pamela B. Schweikert, Director, Compliance Branch (07-Jan-08); Warning Letter to Mr. Phillip L. Carter, President and CEO, Rotech Healthcare, Inc., from Carol A. Heppe, District Director (09-Aug-06); Warning Letter to Ms. Nancy Mavadat, Saint John's Medical Plaza Pharmacy, from Alqiza E. Cruse, Director, Los Angeles District (07-Jan-08).

whose actions raise issues "normally associated with a drug manufacturer."[43] The letters typically cite the Agency's compounding CPG, Section 460.200, which identifies factors that the FDA was to consider as differentiating between traditional compounding, on the one hand, and the manufacturing of new drugs, on the other hand, in determining whether to take enforcement action.[44] The Warning Letters also typically concluded with a warning that failure to promptly correct the issues identified in the letter could "result in additional regulatory action without further notice, including, without limitation, seizure or injunction."

48. In addition, during the time period preceding the fungal meningitis outbreak in 2012, FDA had the authority to recommend a recall and/or issue a "Safety Alert" to healthcare practitioners if it had concerns about the sterility of a drug product that was compounded at a pharmacy.[45]

D. FDA Statements to NECC

49. The Agency may only inspect facilities over which FDA has jurisdiction.[46] In April of 2002, FDA asserted its jurisdiction over NECC by conducting a joint inspection of NECC with the MBP. The inspection stemmed from two MedWatch adverse event reports. FDA again asserted its jurisdiction over NECC by conducting another joint inspection of NECC with the MBP between October 2002 and February 2003. The additional inspection stemmed from three MedWatch adverse event reports concerning preservative-free MPA. Both inspections revealed that NECC had

[43] *See id.*
[44] *See id.*
[45] *See, e.g.*, FDA Safety Alert issued to healthcare providers regarding drugs compounded by NuVision (May 18, 2013)..
[46] *See, e.g.*, FD&C Act § 704.

sterility problems.[47] FDA asserted its jurisdiction over NECC yet again in September of 2004 when it once again inspected the compounding facility.

50. In a Warning Letter to NECC dated December 4, 2006, FDA clearly stated that the Agency had jurisdiction over compounded drugs and the authority to regulate drug manufacturing carried out under the guise of traditional pharmacy compounding. Indeed, FDA stated that its jurisdiction over pharmacy compounding was "supported by substantial judicial authority."[48] The Warning Letter explained:

> FDA has long recognized the important public health function served by traditional pharmacy compounding. FDA regards traditional compounding as the extemporaneous combining, mixing, or altering of ingredients by a pharmacist in response to a physician's prescription to create a medication tailored to the specialized needs of an individual patient. . . . Traditional compounding typically is used to prepare medications that are not available commercially, such as a drug for a patient who is allergic to an ingredient in a mass-produced product, or diluted dosages for children.
>
> Through the exercise of enforcement discretion, FDA historically has not taken enforcement actions against pharmacies engaged in traditional pharmacy compounding. *Rather, FDA has directed its enforcement resources against establishments whose activities raise the kinds of concerns normally associated with a drug manufacturer* . . . .[49]

51. The Warning Letter went on to outline the factors FDA would consider when determining how to "differentiate the traditional practice of pharmacy compounding

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[47] *See, e.g.*, Mass BOP 00915, 00925-26, 00952-53; FDA Form 483 issued to NECC on Feb. 10, 2003.

[48] *See* Warning Letter from Gail Costello, District Director, New England District FDA, to Barry J. Cadden, Director of Pharmacy & Owner, New England Compounding Center (Dec. 4, 2006), at 1 (citing *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 619, 62-30 (1973) (explaining the definition of "new drug"); *Prof'ls & Patients for Customized Care v. Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995) (the FD&C Act does not expressly exempt pharmacies or compounded drugs from its new drug provisions); *In the Matter of Establishment Inspection of: Wedgewood Village Pharmacy*, 270 F. Supp. 2d 525, 543-44 (D.N.J. 2003), *aff'd*, *Wedgewood Village Pharmacy v. United States*, 421 F.3d 263, 269 (3d Cir. 2005) ("The FDCA contains provisions with explicit exemptions from the new drug . . . provisions. Neither pharmacies nor compounded drugs are expressly exempted.")).

[49] *Id.* at 2 (emphasis added).

from the manufacture of unapproved new drugs."[50] These factors included: (1) "whether a firm compounds drugs that are copies or essentially copies of commercially available FDA-approved drug products"; (2) whether, "[l]ike a manufacturer," a firm develops a "standardized . . . drug product" that it markets "by giving physicians . . . free samples" or engaging in other actions that "are not consistent with the traditional practice of pharmacy compounding"; and (3) whether a firm processes and repacks (including repackages) approved drug products, actions "beyond the practice of pharmacy."[51]

52. The Warning Letter specifically asserted that NECC was acting like a drug manufacturer, i.e., it was compounding copies of commercially available drugs, it was developing and marketing standardized drug products, and it was distributing drugs without patient specific prescriptions, and that a number of its drugs did not comply with the FD&C Act. The Warning Letter specially warned NECC that its failure to comply with the FD&C Act could "result in additional regulatory action without further notice, including seizure or injunction[.]"

53. In 2008, FDA sent NECC an additional letter reaffirming the Agency's position that (1) FDA had jurisdiction over pharmacy compounding and (2) the NECC was in violation of the FD&C Act. Based on my review of documents listed in Part II of my report, particularly MBP regulatory documents concerning NECC and FDA regulatory documents concerning NECC, it is clear that FDA remained aware of significant violative conduct at NECC following the issuance of the Warning Letter in 2006 and

[50] *Id.*
[51] *Id.*

the issuance of the letter reaffirming its authority in 2008, yet took no action against NECC.

E. The 2012 Outbreak of Fungal Meningitis

54. Following the 2012 outbreak of fungal meningitis, FDA informed Congress that its authority to take action against NECC was inadequate. Based on my own experience at FDA, the Agency had never before publicly stated that its legal authority over pharmacy compounding was inadequate. The first time it so stated was in response to the stinging criticism from Congress over its abject failure to take any action against NECC prior to the deadly outbreak of fungal meningitis. In light of FDA's prior statements regarding its legal authority to regulate compounding pharmacies like NECC (or, more pointedly, in light of FDA's prior statements regarding its authority to regulate NECC), FDA's claims that it did not have sufficient authority to take an enforcement action against NECC are clearly a post hoc rationalization meant to justify its inaction and to deflect unwanted criticism.

55. That FDA's claims of inadequate authority were patently false was borne out by the complaint the government filed just last week against Downing Labs. There, the government is actually taking action to enjoin a compounding pharmacy's operations for conduct that occurred prior to the enactment of Section 503B based on provisions in the FD&C Act that were in place prior to the enactment of Section 503B; namely it is taking an enforcement action against Downing Labs for compounding drugs (1) under insanitary conditions and (2) without patient-specific prescriptions. It is simply inconceivable, therefore, that FDA could not have used the same provisions in the FD&C Act to have taken an enforcement action against NECC as FDA knew

that NECC was compounding drugs (1) under insanitary conditions and (2) without patient-specific prescriptions.

56. Although Congress in 2013 ultimately gave FDA additional authority in the form of Section 503B, a congressional oversight committee determined that, in fact, FDA had ample authority to take enforcement action against NECC in the months and years preceding the fungal meningitis outbreak.

57. In October 2012, Congress began investigating the fungal meningitis outbreak that was caused by NECC's shipment of contaminated injectable steroid solution to healthcare facilities in 23 states. The purpose of the congressional investigation was to determine "whether this tragedy was preventable had the agency taken action under its existing authorities to address the steady stream of complaints it had received about NECC and its sister company, Ameridose, since issuing a Warning Letter to NECC in December 2006."[52] The Energy and Commerce Committee of the U.S. House of Representatives received briefings from the Centers for Disease Control and Prevention ("CDC"), the Massachusetts Department of Public Health ("MDPH"), and the FDA. On November 14, 2012, the Energy and Commerce Committee's Subcommittee on Oversight and Investigations held a hearing at which several witnesses testified, including FDA Commissioner Margaret Hamburg. (NECC's owner refused to testify, asserting his right against self-incrimination.) Prior

[52] Preliminary Majority Staff Report of the House Comm. on Energy & Commerce, 113th Cong., *FDA's Oversight of NECC and Ameridose: A History of Missed Opportunities?* 2 (Apr. 16, 2013) [hereinafter "*House Report*"], *available at* http://docs.house.gov/meetings/IF/IF02/20130416/100668/ HHRG-113-IF02-20130416-SD101.pdf.

to the hearing, FDA and MDPH produced thousands of pages of documents for congressional investigators to review.

58. At the hearing, Commissioner Hamburg claimed that uncertainty over FDA's authority prevented the Agency from pursuing enforcement actions against companies involved in compounding, including NECC. In her written statement for the Subcommittee's hearing, Commissioner Hamburg asserted that "FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by gaps and ambiguities in the law."[53] In her testimony, Commissioner Hamburg repeatedly mentioned that FDA's authority over compounding pharmacies was questionable, even when such entities were engaged in activities that closely resembled those of a drug manufacturer.[54] As stated previously, never before had I heard anyone at FDA question the Agency's authority to regulate pharmacy compounding—especially where the compounding at issue was in the nature of drug manufacturing.

59. Congressional investigators acknowledged the statements by Commissioner Hamburg and other FDA officials suggesting that FDA's authority to regulate pharmacy compounding was uncertain, but noted that—until the NECC-caused meningitis outbreak—FDA had *always* asserted that it had authority over pharmacy drug compounding. In their report, congressional investigators stated that

> *FDA has long been steadfast in its assertions of authority over drug manufacturing being conducted under the guise of pharmacy*

[53] Statement of Margaret A. Hamburg, M.D., Commissioner, FDA, before the Subcommittee on Oversight and Investigations, U.S. House Committee on Energy and Commerce (Nov. 14, 2012), *available at* http://www.fda.gov/NewsEvents/Testimony/ucm327664.htm.

[54] *See House Report* at 3 (noting that Hamburg stated that "legal framework for FDA activities is very, very unclear, untested, and limited," and that FDA has "ambiguous, fragmented, unclear, and contested authorities in this particular realm of pharmacy and drug manufacturing practice").

> *compounding*—and that the agency would enforce such authority when entities like NECC and Ameridose were engaged in significant violations of the Food, Drug, and Cosmetic Act and jeopardizing public health in the process.[55]

60. Based on their investigation, congressional investigators determined that, in fact, FDA had ample authority to take enforcement action against NECC in the months and years preceding the meningitis outbreak. They determined that

> *at no point in time did the agency lack sufficient authority under the FDCA to take enforcement action against companies that were clearly manufacturing under the guise of compounding and jeopardizing patient safety in the process.* Regardless of whether FDA applied and cited to the factors listed in section 503A or the CPG, NECC and Ameridose were operating well outside the scope of traditional compounding pharmacies and squarely within FDA's authority to take action in response to violations of the FDCA.[56]

Furthermore, congressional investigators determined that although FDA clearly had the authority to take enforcement action against NECC the Agency had failed to do so. Their report states that

> [i]n the six years following the 2006 Warning Letter, FDA failed to take any enforcement action against NECC or Ameridose despite receiving complaint after complaint, often relating to the safety of the companies' drugs. Though several inspections and related enforcement actions were considered during this time period, they were repeatedly delayed and ultimately cancelled. In fact, in 2011, FDA made an affirmative decision to suspend inspections and enforcement actions relating to compounding operations, including NECC and Ameridose, until the agency finalized new guidance to industry detailing where it would draw the line between pharmacy compounding and drug manufacturing. Regardless of where this line would ultimately have been drawn, based on a review of the documents, it appears evident that NECC and Ameridose had already crossed it.[57]

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[55] *Id.* at 3 (emphasis added).
[56] *Id.* at 6-7 (emphasis added).
[57] *Id.* at 3.

61. In their *House Report*, congressional investigators concluded that FDA's failure to take enforcement action against NECC was not because FDA lacked the authority to take such action:

> FDA's recent decisions not to even re-inspect NECC or Ameridose pursuant to any of the complaints the agency received are perplexing, *particularly in light of FDA's flurry of enforcement activity since the meningitis outbreak involving a number of companies engaged in similar practices*. According to FDA, since October 1, 2012, the agency has inspected 50 compounding facilities—issuing Form 483s to approximately 30 firms, resulting in five firms recalling their products, and one firm receiving a Warning Letter. FDA staff informed Committee staff that other regulatory actions are under consideration. . . . *Prior to these inspections taking place, no new laws were passed and no new regulations or guidance documents were issued.*[58]

In sum, based on a thorough investigation that included briefings, a hearing, and review of thousands of pages of documents, a congressional oversight committee determined that, prior to the NECC-caused meningitis outbreak in 2012, FDA had authority to regulate the sort of compounding in which NECC was engaged. In my opinion, if FDA had exercised its enforcement authority over NECC (which it viewed as a drug manufacturer), the fungal meningitis outbreak of 2012 would not have occurred.

[58] *Id.* at 3-4 (emphases added).

I declare under penalty of perjury of the laws of the United States that the above is true and correct and that this document was executed on January 15, 2016, in Washington, D.C.

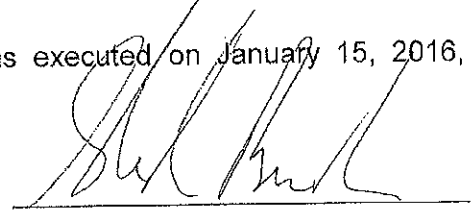

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EXHIBIT 1

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In October 2007, Sheldon Bradshaw joined Hunton & Williams LLP as a partner and co-chair of the firm's Food and Drug Practice Group. Mr. Bradshaw came to the firm from the U.S. Food and Drug Administration (FDA), where he served as Chief Counsel. As Chief Counsel, Mr. Bradshaw was responsible for providing legal advice to the Secretary and Deputy Secretary of the U.S. Department of Health and Human Services and to the FDA's senior leadership -- including the Commissioner, the Deputy Commissioners and the Directors of the various FDA Centers -- on issues related to drugs, biologics, medical devices, food, animal feed and drugs, cosmetics, dietary supplements and other products regulated under the Federal Food, Drug and Cosmetic Act and the Public Health Service Act. In addition, he oversaw all FDA-related litigation and reviewed and approved every significant regulation and guidance document promulgated by the FDA and every significant warning letter issued by the FDA. Prior to his service at the FDA, Mr. Bradshaw held several senior positions at the U.S. Department of Justice where he, among other things, provided advice to FDA and testified before Congress on matters under the FDA's jurisdiction. At the firm, Mr. Bradshaw advises clients in the same areas in which he worked while Chief Counsel of FDA.

Relevant Experience

- Advised numerous pharmaceutical companies on drug approval strategies involving new drug applications (NDAs) under 505(b)(1) and 505(b)(2), suitability petitions, and abbreviated new drug applications (ANDAs) under 505(j).
- Counseled clients regarding product life cycle management (including the development of new products and line extensions), Hatch-Waxman issues (including patent and non-patent exclusivities, 30-month stays, labeling carve outs and FDA's Orange Book); user fees, and risk evaluation and mitigation strategies (REMS).
- Assisted pharmaceutical companies and device manufactures with post-approval issues, including labeling changes, adverse event reporting, compliance with current good manufacturing practices (cGMPs), data integrity issues and promotional activities.
- Helped clients respond to, and recover from, Warning and Untitled Letters sent by FDA, most of which involved alleged cGMP violations or violative promotional materials.
- Negotiated consent decree with the FDA stemming from cGMP violations and data integrity issues.
- Counseled clients regarding advertising and promotion issues related to FDA-regulated products, including representing clients before the FDA and reviewing product marketing materials for compliance with FDA regulations.

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- Represented several clients in disputes with competitors regarding the unlawful advertising and promotion of drug products and medical devices. Submitted trade complaints to FDA objecting to such promotional activities.
- Provided legal and regulatory advice related to numerous product recalls involving prescription and over-the-counter drug products and food products.
- Advised device manufacturers on 510(k) and pre-market approval (PMA) applications.
- Advised clients regarding "intended use" and the types of claims that distinguish drugs and devices from cosmetics, dietary supplements and food.
- Reviewed labeling of drugs, both Rx and OTC, devices, dietary supplements, food, and cosmetics for compliance with the FD&C Act.
- Counseled clients on legal issues related to the design and implementation of clinical trials, including the preparation of investigational new drug (IND) applications and investigational device exemption (IDE) applications and the submission of information to the clinical trial registry and the new clinical trial results database.
- Provided clients with crisis management counseling on product recalls, government inspections and seizures, data integrity issues, adverse events, import alerts and similar issues.
- Advised clients on issues related to the practices of medicine and pharmacy.
- Represented companies in interactions with regulatory officials from the FDA.
- Assisted companies in criminal, civil, and administrative enforcement actions and related civil litigation involving health care fraud and abuse, qui tam lawsuits, preemption, data integrity, off-label promotion, misbranding, adulteration, and the anti-kickback statute.
- Advised clients on issues related to pharmacy compounding and the distinction between traditional pharmacy compounding and manufacturing.
- Retained as an expert witness in numerous cases, including the following:
    - Lawsuit involving allegations that the advertising for a cosmetic rendered the product a drug under the FD&C Act.
    - Three different lawsuits involving FDA's juice labeling regulations and the FDA Warning Letter process..
    - Lawsuit involving the FDA's Pre-Launch Activities Importation Request ("PLAIR") program.
    - Arbitration involving the FDA's use of Import Alerts.

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- Lawsuit involving FDA's review of proprietary drug names.
- Lawsuit involving animal drug compounding.
- Two different lawsuits involving application of the Hatch-Waxman Amendments.
- Four different lawsuits involving FDA's regulation of drug labeling, advertising and marketing.
- Advised several pharmaceutical companies subject to FDA's Application Integrity Policy (AIP) with data integrity issues.
- Counseled a client importing food products that were subject to a country-wide Import Alert.
- Assisted pharmaceutical and cosmetic companies in removing products from an Import Alert.
- Advised pharmaceutical companies with manufacturing facilities subject to Import Alerts.
- Represented a client in negotiations with the FDA over the importation of medical devices.
- Drafted Citizen Petition submitted to FDA.
- Submitted comments on behalf of clients to several FDA dockets.
- Represented numerous large, mid-sized, and emerging pharmaceutical, biotechnology, and medical device companies in regulatory matters involving product development and commercialization.

Background

- Chief Counsel, U.S. Food and Drug Administration, 2005-2007
- Principal Deputy Assistant Attorney General, Civil Rights Division, U.S. Department of Justice, 2003-2005
- Deputy Assistant Attorney General, Office of Legal Counsel, U.S. Department of Justice, 2001-2003
- Associate, Howrey Simon Arnold & White, 1999-2001
- Law Clerk, Hon. Karen J. Williams, U.S. Court of Appeals for the Fourth Circuit, 1996-1999

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Membership

- Member, District of Columbia and Montana State Bars
- Member, United States Court of Appeals for the Fourth Circuit; United States Court of Appeals for the Fifth Circuit; United States District Court for the District of Columbia
- Member, Food and Drug Law Institute

Speeches

- Speaker, FDLI Annual Conference 2015, "Center for Biologics," Washington, DC, April 20-21, 2015.
- Speaker, George Mason University's Law & Economics Center, "The FDA's Proposed Rule for Generic Drug Liability," Washington, DC, February 24, 2014.
- Speaker, GPhA Annual Meeting, "GDUFA: Promise & Progress," Orlando, FL, February 20, 2014.
- Moderator, FDLI 56th Annual Conference, "Center for Veterinary Medicine," Washington, DC, April 23, 2013.
- Speaker, University of North Carolina Medical School, "Legal Life Skills for Physicians," Chapel Hill, NC, March 19, 2013.
- Speaker, FDA In-House Training, "Violations and Enforcement," Silver Spring, MD, February 22, 2013.
- Speaker, 8th Annual Nutrition Law Symposium, "FDA Update – Enforcement 2012: Things You Need To Know," Lehi, UT, September 14, 2012.
- Speaker, FDLI 55th Annual Conference, "Former FDA Chief Counsels Roundtable," Washington, DC, April 25, 2012.
- Speaker, FDA In-House Training, "Regulation of Drug Marketing," Silver Spring, MD, March 9, 2012.
- Speaker, VBDC Entrepreneurial Luncheon Series, "FDA-102: Recent Developments Impacting Life Sciences Entrepreneurs," Richmond, VA, November 11, 2010.
- Speaker, FDA In-House Training, "Regulation of Drug Marketing," "Violations and Enforcement," "Regulation of Drug Manufacturing," Product Liability," "Post-Approval Obligations of Applicants," and "FDA' Regulatory Processes," Silver Spring, MD, October 19, 2010.
- Speaker, Thompson Audio Conference, "The Park Doctrine: Protect Yourself," July 27, 2010.

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- Speaker, Expert Briefing, "Consent Decrees," On-line presentation, June 17, 2010.
- Speaker, FDLI 53rd Annual Conference, "Animal Drug Compounding," Washington, DC, April 22, 2010.
- Speaker, FDA In-House Training, "Violations and Enforcement," Silver Spring, MD, March 17, 2010
- Speaker, FDA Enforcement Tools, "Update on FDA's New 'Aggressive' Enforcement Policies," On-line presentation, December 3, 2009
- Speaker, Portrait Dedication Ceremony for The Honorable Karen J. Williams, United States Court of Appeals for the Fourth Circuit, Recognition Remarks, Richmond, VA, December 2, 2009
- Speaker, University of Maryland School of Law's Conference on Emerging Issues in Food & Drug Law, "Preemption," Baltimore, MD, November 16, 2009
- Speaker, Virginia Biosciences Development Center "Brown Bag" Luncheon Seminar Series, "FDA-101: A Current Update for Life Sciences Entrepreneurs," Richmond, VA, November 12, 2009
- Speaker, FDLI Tobacco Legislation and Regulation Conference, "Family Smoking Prevention and Tobacco Control Act of 2009," Washington, D.C., November 10, 2009
- Speaker, Expert Briefing, "Trends in Warning and Untitled Letters," On-line presentation, November 10, 2009
- Speaker, FDA Enforcement Tools, "Update on FDA's New 'Aggressive' Enforcement Policies," On-line presentation, October 6, 2009
- Speaker, 4th FDA Regulatory and Compliance Symposium, "New Directions in Federal Preemption," Washington, DC, September 30, 2009
- Speaker, FDA Commissioner's Fellowship Program, "Origins and Overview of the Organizational Structure of FDA and the Regulation of Drugs," Silver Spring, MD, July 16, 2009
- Speaker, ACI's 9th National Conference, "Dissemination of Off-Label Materials: Minimizing Liability Risks of Off-Label Promotion," Chicago, IL, June 9, 2009
- Speaker, Bio Conference, "The Emerging Promise of Personalized Medicine," Atlanta, GA, May 19, 2009
- Speaker, FDLI Annual Conference, "Preemption," Bethesda, MD, April 23, 2009
- Speaker, FDA Boot Camp, "Drugs, Biological, and Medical Device Products: Labeling," New York, NY, March 30, 2009

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Food and Drug

- Speaker, Clinical Trials, "Mastering Clinicaltrials.gov: Developing Proficiency with the Program, Protecting Your Data and Managing Costs and Time," New York, NY, February 24, 2009
- Speaker, "FDA Briefing on Preemption and Its Implications for Patients, Physicians, and Industry", December 18, 2008
- Speaker, "Expert Briefing: What the Pharmaceutical Industry Needs to Know About the Expanded Clinical Trial Registry and the New Clinical Trial Results Database," On-line Presentation, November 12, 2008
- Speaker, "FDA Preemption: Legal Issues in Wyeth," On-line Presentation, November 6, 2008
- Speaker, Developments in Drug Safety Conference: "FDAAA Enforcement: Defining How the FDA will Hold Pharmaceutical Companies Accountable for Meeting FDAAA Post-Approval Requirements," Washington, D.C., October 20-21, 2008
- Speaker, ACI FDA Boot Camp: "Drugs and Biological Products: Labeling," Boston, MA, September 22-23, 2008
- Speaker, 2008 Nutritional Law Symposium: "An Inside View of Regulatory and Enforcement Trends Affecting Dietary Supplements," Salt Lake City, UT, September 12, 2008
- Speaker, Expert Briefings: "Trends in Warning and Untitled Letters -- What the Pharmaceutical Industry Needs to Know," On-line Presentation, August 12, 2008
- Speaker, ACI Drug and Device Preemption Conference: "Examining the FDA's Current Preemption Goals and Priorities," Philadelphia, PA, July 14-15, 2008
- Speaker, "New GMP Compliance Requirements Under FDAAA 2007," On-line Presentation, May 28, 2008
- Speaker, CBI's Drug Tracking Summit: "Insight into the FDA's Initiatives to Protect the Supply Chain," Princeton, NJ, May 15, 2008
- Speaker, Personal Care Products Council's Legal and Regulatory Conference: "The State of FDA: Perspectives from Former Chief Counsels," Chicago, IL, May 10, 2008
- Speaker, "CMS and FDA Policies on Clinical Trials," Bethesda, MD, May 8, 2008
- Speaker, "Understand the Critical Elements of the FDA Amendments Act of 2007," Washington, D.C., March 10, 2008

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- Speaker, 9th National Conference on Managing Legal Risks in Structuring and Conducting Clinical Trials: "FDA Amendments Act of 2007: Overcoming Implementation Issues with Respect to Clinical Trial Registry and Post-Approval Safety," New York City, NY, February 26, 2008
- Speaker, "Annual Meeting of the Food, Drug and Cosmetic Law Section," New York State Bar Association, New York, NY, January 31, 2008
- Speaker, "Drawing the Line Between Physician Education and Product Promotion: Charting a Course for Policy Reform," Seton Hall Law, Newark, NJ, January 30, 2008
- Speaker, "Biosimilars - Where Are We Now? Where Are We Going?" American Intellectual Property Law Association 2008 Mid-Winter Institute, Phoenix, AZ, January 24, 2008
- Speaker, "Generics: User Fees, Citizen Petitions and Authorized Generics," JPMorgan Healthcare Conference, Washington, D.C., December 18, 2007
- Moderator, "US Regulation of Combination Products," AHLA Life Sciences Practice Group, Washington, D.C., December 6, 2007
- Moderator, "Citizen Petitions," FDLI's Program on FDA Implementation of the New Law - The Food and Drug Administration Amendments Act of 2007, Washington, D.C., November 16, 2007
- Speaker, "An Insider's Views of the FDA: 'Is It Always Raining on Me?'": New York Pharma Forum, New York, NY, November 12, 2007
- Speaker, "Preemption Under the Food, Drug & Cosmetic Act," 4th Annual Drug and Medical Device Litigation, New York, NY, November 1, 2007
- Speaker, "2007 FDA Legal and Policy Challenges" GPhA's 2007 Annual Policy Conference, Washington, D.C., September 6, 2007
- Speaker, "Achieving Quality Through Compliance: Understanding the FDA's Viewpoint on Compliant Medical Education," CBI's 7th Annual Medical Education Conference, Philadelphia, PA, June 2007
- Speaker, "Preemption: How the FDA Views Preemption," Drug and Medical Device Seminar, San Francisco, CA, May 10, 2007
- Speaker, "FDA's Viewpoint on Industry-Supported Medical Education," 2007 MedEd Conference, Philadelphia, PA, May 3, 2007
- Speaker, "New FDA Guidance Documents on Unapproved Drugs and Communicating Risk Information," FDLI Annual Conference, Washington, D.C., April 12, 2007

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Food and Drug

- Speaker, "Meeting With The FDA Chief Counsel," PhRMA Bi-Annual Meeting, Washington, D.C., April 11, 2007
- Speaker, "FDA's Regulatory Agenda" CBI's 4th Annual Pharmaceutical Marketing Congress, Washington, D.C., January 29, 2007
- Speaker, "FDA's Perspective on Dietary Supplements and the Industry" Nutritional Law Symposium, Lehi, Utah, September 22, 2006
- Speaker, "FDA's Perspective on Dietary Supplements and the Industry" Council for Responsible Nutrition, Covington & Burling, Washington, D.C., December 7, 2006
- Speaker, "The Federal Government's Role in Protecting Our Food Supply" DRI Food Law Seminar, Chicago, IL, November 9, 2006
- Speaker, FDLI "Emerging Issues Concerning Nutrition and Health Claims" Food Labeling Claims and Controversies, Washington, D.C., October 31, 2006
- Speaker, "The Path Forward for Functional Foods" Food Policy Symposium, Univ. of Mass, Amherst, MA, October 25, 2006
- Speaker, "Legal Issues Affecting the Generic Drug Industry," GPhA's 2006 Annual Policy Conference, Washington, D.C., September 19, 2006
- Speaker, "An Overview of FDA's Regulatory Compliance Agenda," FDA Regulatory and Compliance Symposium, Harvard Univ., Boston, MA, August 25, 2006
- Speaker, "Preemption," PhRMA, Member Lawyers, Washington, D.C., July 28, 2006
- Luncheon Speaker, "Origins of the Pure Food and Drug Act of 1906," Covington & Burling, Washington, D.C., June 12, 2006
- Panelist, "GC Roundtable - Health Lawyering from the Inside," ABA Health Law Section, Washington, D.C., May 24, 2006
- Speaker, "Current Agency Issues," PhRMA FDA Focus Group Meeting, Jefferson Hotel, Washington, D.C., March 7, 2006
- Speaker, "Citizen Petition Process," CitiGroup Healthcare Conference, Mayflower Hotel, Washington, D.C., February 27, 2006
- Panelist, LDS Law Student Conference, Georgetown University, Washington, D.C., February 18, 2006
- Speaker, "General Counsel Series - Transition to FDA, OCC Office Functions, Current Agency Activities," DC Bar Administrative Law and Agency Practice Section, Washington, D.C., February 9, 2006

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Food and Drug

- Speaker, "Meet the Regulators," CTFA Conference, Washington, D.C., February 1, 2006
- Panelist, "Federal Regulatory Panel," ANA Annual Advertising Law and Business Affairs Conference, New York, NY, January 25, 2006
- Speaker, "Current Issues Impacting the Generic Pharmaceutical Industry," Morgan Stanley Global Generic Pharmaceuticals Seminar, New York, NY, January 6, 2006
- Panelist, "Regulators Roundtable" Sixth Pharmaceutical Regulatory Compliance Congress, Washington, D.C., November 8, 2005
- Speaker, Pharmaceutical Representatives APCO Worldwide, Washington, D.C., October 20, 2005
- Speaker, "New Directions in Drug Safety," ABA Program on Health Law, Washington, D.C., October 20, 2005
- Speaker, "Origins of the Pure Food and Drug Act of 1906," FDA Alumni Association, Gaithersburg, MD, October 15, 2005
- Speaker, GPhA's "Legal Issues Affecting the Generic Drug Industry," 2005 Annual Policy Conference, Washington, D.C., September 19, 2005
- Speaker, "OCC Focus," ORA DCB/DIB Conference, ORA University, Rockville, MD, September 13, 2005

Publications

- Co-author, FDA's Proposed Generic Drug Labeling Rule, *FDLI's Update Magazine*, July/August 2014
- Co-author, New Compounding Legislation, *Contract Pharma*, January/February 2014
- Co-author, A Compounding Fracture at the FDA, *The Wall Street Journal*, November 13, 2012
- Co-author, Did FDA Apply a Remedy Worse than the Disease in Refusing to Clear the Market of Unapproved Versions of Makena? *FDLI's Food and Drug Policy Forum*, Volume 1, Issue 11, June 2011
- Co-author, The FDA's Approval of Percocet and Vicodin, *Law360*, July 15, 2009
- Co-author, FDA Enforcement Crackdown Requires Reforms, *Law360*, June, 30, 2009
- Co-author, "FDA: playing by its own rules?," *Scrip World Pharmaceutical News*, November 7, 2008

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Sheldon T. Bradshaw
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- Author, New FDA Guidance Documents, 62 *Food and Drug Law Journal* 429-432, 2007

Education

- J.D., George Washington University Law School, with honors, Managing Editor, *The George Washington Law Review*, Dean's Fellow, 1996
- B.A., Brigham Young University, Political Science, 1991

EXHIBIT "B"

HENRY I. MILLER, MD

Henry I. Miller, M.D.

I. Qualifications

I am currently the Robert Wesson Fellow in Scientific Philosophy and Public Policy at the Hoover Institution at Stanford University. I earned my undergraduate degree, a bachelor of science, from the Massachusetts Institute of Technology (M.I.T.) in Cambridge, Massachusetts. I earned my medical degree (M.D.) and a master's degree (M.S.) in Molecular Biology from the University of California, San Diego in 1975. I successfully completed post-graduate internship, residency, and fellowship training in the Department of Medicine at Harvard Medical School's Beth Israel Hospital in Boston Massachusetts from 1975 to 1977.

From 1977 to 1979, I served as a research associate at the National Institutes of Health's National Institute of Child Health and Human Development in the Laboratory of Molecular Genetics. My research focused on the study of gene organization and expression.

From 1979 to 1994, I was employed by the Food and Drug Administration ("FDA") in a number of different roles. From 1979 to 1983, I devoted ten (10) percent of my time as a Health Scientist Administrator in the Office of Recombinant DNA Activities at the National Institutes of Health, and ninety (90) percent of my time as a Medical Officer within the Division of Metabolism and Endocrine Drug Products at the Center for Drugs and Biologics of the FDA, focusing primarily on activities related to new biotechnology, including policymaking and review of submissions to the FDA. From 1983 to 1985, I worked as a Medical Officer within the Office of Biologics in the Center for Drugs and Biologics, FDA, focusing on activities related to new drug development, including policymaking and review of submissions to the FDA. From 1980 to 1985, on

several occasions, I accompanied other FDA personnel on inspections of manufacturing facilities.

From 1985 to 1989, I worked as the Special Assistant to the Commissioner of Food and Drugs, the head of the FDA. My responsibilities included providing staff support and advice to the Commissioner and other divisions of the FDA, undertaking policy-making initiatives, representing the FDA's interests, and providing expertise on intra- and extra-governmental panels and working groups in the United States and abroad. From 1989 to 1993, I served as the Director of the Office of Biotechnology, which was the principal policy-making entity at the FDA for all new biotechnology products. In this role, I served as the FDA's contact person for the Securities and Exchange Commission for vetting claims by companies about likely regulatory approvals.

My work at the FDA from 1990 to 1993 overlapped with the tenure of David A. Kessler, MD. In 1991, I witnessed Dr. Kessler's diversion of significant staff and field resources in the aggressive seizure of 15,000 gallons of Citrus Hill orange juice made from concentrate, only because it was labeled "fresh." In 1992, I witnessed Dr. Kessler's implementation of a moratorium on the availability of silicone gel breast implants, bankrupting Dow Corning and requiring the surviving manufacturers of silicone breast implants to spend billions of dollars defending lawsuits and funding mass-tort settlements based on unreliable scientific information embraced by Dr. Kessler. During the tenure of Dr. Kessler, the FDA followed many fundamentally flawed priorities. I understand that Dr. Kessler left the FDA without having another professional position

arranged, reportedly due to irregularities in travel reimbursements and use of FDA funds.

Since leaving the FDA in 1994, I have served as the Robert Wesson Fellow in Scientific Philosophy and Public Policy at the Hoover Institution at Stanford University in Stanford, California. My research focuses on public policy issues pertaining to risk and its regulation with a special emphasis on pharmaceutical development and biotechnology. Additionally, I served as a Distinguished Fellow with the Public Health Policy Advisory Board from 2005 to 2008.

A copy of my *curriculum vitae*, more fully setting forth my experience and professional accomplishments, is attached as Exhibit 1. Any publications I have authored in the previous ten (10) years are listed on my *curriculum vitae* and/or on my webpage on the Hoover Institution's website, http://www.hoover.org/profiles/henry-i-miller.

II. Materials Considered in Forming Opinions

In forming my opinions, I relied on my education, training, experience, and the materials I reviewed, including the following:

1. Massachusetts Board of Pharmacy documents concerning NECC cited in the text of my report. The attached CD contains the Bates stamped documents.
2. FDA regulatory documents concerning NECC cited in the text of this report. The attached CD contains the Bates stamped documents.
3. The Complaint from the *Reed* case.
4. 2002-2003 FDA Establishment Inspection Report of NECC.

5. Heinrich J., Prescription Drugs – State and Federal Oversight of Drug Compounding by Pharmacies, US General Accounting Office, GAO-04-195T, Oct. 23, 2003, http://www.gao.gov/assets/120/110456.pdf (Attached as Exhibit 2).
6. FDA Compliance Policy Guide Section 7132.16 – March 1992.
7. FDA Compliance Policy Guide Section 460.200 – May 2002.
8. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et al.*
9. 21 C.F.R. § 2.5.
10. Exhibits to and Transcript of the Deposition of Samuel Penta testifying as the Massachusetts Board of Pharmacy.
11. Kay Lazar, *State pharmacy officials knew convict led oversight firm*, Boston Globe, November 13, 2012 (Attached as Exhibit 3).
12. Kay Lazar & Liz Kowalczyk, *State was lax on Framingham drug maker*, Boston Globe, November 14, 2012 (Attached as Exhibit 4).
13. Inside Washington Publishers, *Galderma: Unapproved Drug Makers Must Tell Doctors Drug's Status*, January 2, 2004 (Attached as Exhibit 5).
14. April 2011 Institute for Safe Medication Practices publications (Attached as Exhibits 6 and 7).
15. The Pharma Letter, *FDA warning letters rise 78% over six years with increase expected in 2015*, http://www.thepharmaletter.com/article/fda-warning-letters-rise-78-over-six-years-with-increase-expected-in-2015 (Attached as Exhibit 8).

16. April 2011 Colorado Board of Pharmacy Cease and Desist Order applicable to NECC.
17. July 20, 2012 Colorado Board of Pharmacy Special Report regarding NECC.
18. Colorado Board of Pharmacy communications by e-mail with the New England District Office of the FDA regarding NECC.
19. November 2012 Congressional Testimony of Margaret A. Hamburg, FDA Commissioner, and Lauren Smith, Massachusetts Department of Public Health Interim Commissioner.
20. February 1, 2013 letter from the House of Representatives to the FDA.
21. April 16, 2013 House of Representatives Staff Report: "FDA's Oversight of NECC and Ameridose: A History of Missed Opportunities?"
22. May 22, 2013 Senate Committee Staff Report: "The Case for Clarifying FDA Authority: Large-Scale Drug Compounding and the Ongoing Risk to Public Health."
23. Second Amended Master Complaint.
24. STOPNC, *et al.*'s Master Answer.
25. David A. Kessler, MD's Rule 26 Disclosure.

I may use these materials as exhibits to support my opinions. My understanding is that additional information relevant to my opinion may become available in the future, through depositions or the criminal trial of individuals associated with NECC, and ongoing production of documents. I reserve the right to amend or supplement this report.

III. Facts and Data Considered in Forming My Opinions

The following summarizes the facts I rely upon in forming my opinions regarding the claims made against Saint Thomas Outpatient Neurosurgical Center ("STOPNC"), John Culclasure, MD, Debra Schamberg, RN, CNOR, and Vaughan Allen, MD.

A. Background of STOPNC and Howell Allen Clinic

Howell Allen Clinic and Saint Thomas Network, formerly known as Saint Thomas Health Services, opened St. Thomas Outpatient Neurosurgical Center ("STOPNC") in 2000 as an ambulatory surgery center. Each entity owned 50% of STOPNC. When it opened, STOPNC was used almost exclusively as an operating room, performing occasional pain management procedures. In 2005, STOPNC began focusing on pain management procedures, and now, the facility does exclusively pain management. STOPNC is accredited by the Joint Commission as an ambulatory surgery center. Howell Allen is a neurosurgical group in Nashville that refers patients to STOPNC, and to Premier Orthopedics, for pain management.

John W. Culclasure, MD is an employee-anesthesiologist at Howell Allen. He is STOPNC's Medical Director. Dr. Culclasure received his medical degree from the Medical University of South Carolina in 1983. He completed his post-graduate residency in anesthesiology at Walter Reed Medical Center, followed by service on active duty for six years and seven months in the U.S. Army Medical Corps as an officer. Dr. Culclasure received an honorable discharge in 1990. After leaving the Army, Dr. Culclasure's practice continued to focus primarily on anesthesia for the next several years. In the early 90s, he began to practice more in pain management, and his practice gradually shifted to focus almost entirely on pain management. Dr. Culclasure joined

Howell Allen in 2005. He performs the majority of the pain management procedures at STOPNC. Dr. Culclasure has served as STOPNC's Medical Director since 2005. He is also an Adjunct Associate Professor in the Department of Anesthesiology at Vanderbilt University School of Medicine.

Debra Schamberg, RN, CNOR is STOPNC's Facility Director. Ms. Schamberg graduated from Tennessee State University School of Nursing in 1984. She was an OR nurse for the majority of her career. When she was hired by Howell Allen to work at STOPNC in 2000, she began to take on more management and administrative responsibilities, such as monitoring safety compliance, writing and revising policies and procedures, and teaching and orienting new employees. In 2005, when STOPNC began focusing on pain management, Howell Allen transferred Ms. Schamberg to the Center for Spinal Surgery, another facility in which Howell Allen maintained an ownership interest. At the Center for Spinal Surgery, she worked as an OR nurse, the OR Educator, the Infection Control Nurse, and the Employee Health Nurse. In May 2009, Ms. Schamberg became STOPNC's Facility Director.

a. STOPNC's Relationship with NECC

STOPNC purchased preservative-free methylprednisolone acetate ("MPA") from NECC for the first time in June 2011, and began administering it to patients shortly thereafter. The primary reason STOPNC began purchasing from NECC was that NECC could provide a guaranteed supply of preservative-free MPA. In early to mid-2011, Ms. Schamberg learned that there was a backorder or impending shortage of single-dose vials of MPA from STOPNC's current suppliers. In the same timeframe, Dr. Culclasure

was interested in securing MPA without preservative because of reports of adverse events following epidural injections with steroids containing preservatives.

In mid-2011, Sandra Littleton, RN, a nurse at STOPNC involved in ordering MPA, and Ms. Schamberg, learned in their discussions with representatives of Clint Pharmaceuticals and/or CuraScript (suppliers of MPA) that MPA was on shortage or backorder status. A NECC sales representative, John Notarianni, assured Ms. Schamberg that NECC would always be able to fill STOPNC's orders for MPA, and that STOPNC would not have to deal with backorders or shortages of MPA if STOPNC purchased from NECC.

STOPNC placed its first order for MPA from NECC on either June 10 or June 14, 2011.[1] NECC shipped the order on June 16, 2011. NECC was STOPNC's sole supplier of MPA from that point until the fungal meningitis outbreak. There were no problems with any medication STOPNC received from NECC prior to the fungal meningitis outbreak. The quality of the medication appeared excellent. The orders STOPNC placed were delivered promptly and on-time. As promised by John Notarianni, STOPNC no longer had to deal with shortages of MPA.

b. 2012 Fungal Meningitis Outbreak

In the fall of 2012, public health officials in Tennessee were alerted to a case of fungal meningitis caused by *Aspergillus fumigatus*. The source of the contamination was eventually narrowed down to three (3) lots of MPA compounded by NECC. *After the outbreak, multiple state and federal agencies and accrediting or licensing bodies, including the FDA, CDC, Tennessee Department of Health, and Joint Commission,*

[1] It appears there was an error in transmission of the order on June 10, 2011, that was not discovered and remedied until June 14, 2011.

conducted investigations of the outbreak and found no wrongdoing on the part of healthcare providers who purchased from NECC.

B. FDA Regulatory Authority

a. FDA Compliance Policy Guide Section 7132.16

On March 16, 1992, the FDA issued Compliance Policy Guide ("CPG") Section 7132.16 (subsequently renumbered as 460.200) on pharmacy compounding. The FDA reissued Section 460.200 on May 29, 2002. CPG Section 460.200 was withdrawn on December 4, 2013, but was in effect in 2012 when NECC compounded the contaminated MPA at issue. Section 460.200 provided, in pertinent part:

> Generally, FDA will continue to defer to state authorities regarding less significant violations of the [Food, Drug, and Cosmetic] Act related to pharmacy compounding of human drugs. FDA anticipates that, in such cases, cooperative efforts between the states and the Agency will result in coordinated investigations, referrals, and follow-up actions by the states. However, when the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new drug, adulteration, or misbranding provisions of the [Food, Drug, and Cosmetic] Act, FDA has determined that it should seriously consider enforcement action. In determining whether to initiate such an action, the Agency will consider whether the pharmacy engages in any of the following acts:
>
> 1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions....
>
> 8. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products.[2]

[2] FDA CPG § 460.200 (2002).

b. FDA "Imminent Hazard to the Public Health"

Under 21 C.F.R. § 2.5, the FDA has authority to take action against a product or practice as an "imminent hazard to the public health," which exists when the following is met:

> [T]he evidence is sufficient to show that a product or practice, posing a significant threat of danger to health, creates a public health situation (1) that should be corrected immediately to prevent injury and (2) that should not be permitted to continue while a hearing or other formal proceeding is being held...The occurrence of the final anticipated injury is not essential to establish that an *imminent hazard* of such occurrence exists....In exercising his judgment on whether an *imminent hazard* exists, the Commissioner will consider the number of injuries anticipated and the nature, severity, and duration of the anticipated injury.[3]

c. Federal Food, Drug, and Cosmetic Act

Section 353a of the Federal Food, Drug, and Cosmetic Act ("FDCA") provides a "safe harbor" for pharmacy compounders, exempting compounders from the "new drug" approval, adulteration, and misbranding provisions of the FDCA under the following conditions:

> The drug product is compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding –
>
> (1) is by –
>
> (A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or
>
> (B) a licensed physician, on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

[3] 21 C.F.R. § 2.5 (2015).

> (2)(A) is by a licensed pharmacist or a licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and
>
> (B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between—
>
> (i) the licensed pharmacist or licensed physician; and
>
> (ii)(I) such individual patient for whom the prescription order will be provided; or
>
> (II) the physician or other licensed practitioner who will write such prescription order.[4]

C. 2003 GAO Senate Testimony

On October 23, 2003, the Director of Health Care and Public Health Issues for the United States General Accounting Office, Janet Heinrich, testified before the Senate Committee on Health, Education, Labor, and Pensions regarding state and federal oversight of pharmacy drug compounding.[5] The FDA did not require pharmacies to report adverse events associated with compounded drugs, but learned of adverse events from voluntary reporting, media reports, and other sources. Notably, Ms. Heinrich testified that, *since 1990, the FDA knew of over 200 adverse events involving 71 compounded products, including three (3) deaths and 13 hospitalizations resulting from injections of contaminated compounded medication in 2001.*[6]

The FDA maintained that drug compounding activities were generally subject to FDA oversight, including the "new drug" requirements and other provisions of the

[4] 21 U.S.C.A. § 353a.
[5] Exhibit 2.
[6] *Id.* at 4.

FDCA.[7] The FDA's "primary concern" was situations in which drug compounding was conducted in a way that constituted "manufacturing," but attempted to circumvent the FDCA's "new drug" requirements.[8] The FDA provided in its CPG § 460.200 that it should seriously consider enforcement action when the scope and nature of a pharmacy's activities raise the types of concerns normally associated with drug manufacturers, resulting in significant violations of the FDCA, including compounding commercially available drugs or using "commercial scale manufacturing or testing equipment."[9] Ms. Heinrich testified that a New Jersey District Court believed that the FDA's CPG § 460.200 was a "reasonable interpretation of the statutory scheme established by the FDCA."[10]

The FDA generally relied on states to regulate traditional compounding. Unfortunately, the ability of states to oversee and ensure the quality and safety of compounded drugs may be affected by state-specific factors, including limitations of the resources available for inspections and enforcement.[11] In three (3) of the four (4) states reviewed by the GAO, pharmacy board officials stated that resource limitations affected their ability to conduct routine inspections of compounding pharmacies.[12]

Ms. Heinrich testified that the FDA did not routinely collect data on the quantity of prescriptions filled by compounded drugs, and the GAO did not find any publicly available data on the amount of bulk active ingredients and other chemicals used in drug compounding in the United States.[13]

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[7] *Id.* at 9.
[8] *Id.* at 10.
[9] *Id.* at 11.
[10] *Id.* at 12.
[11] *Id.* at 2.
[12] *Id.*
[13] *Id.* at 4.

D. 2003 Galderma Survey

In November 2003, Galderma, a dermatologic drug company, surveyed 165 dermatologists to assess their perceptions of medications not approved by the FDA.[14] Eighty-five (85) percent of the 165 healthcare providers surveyed reported that they believed *all* prescription drugs were approved by the FDA.[15] Eighty-five (85) percent of the healthcare providers stated that physicians should be able to determine whether the FDA has approved a drug product, and seventy-five (75) percent of the providers stated that it would be helpful for this information to be disclosed in labeling.[16]

E. 2011 ISMP Publications

In April 2011, the Institute for Safe Medication Practices ("ISMP") published two (2) articles calling for greater FDA guidance and state pharmacy board oversight of sterile compounding.[17] ISMP issued the following recommendations to improve the safety of compounded medications:

> 1) All state boards of pharmacy should expect compounding pharmacies to comply with all aspects of [USP] Chapter 797, and survey these pharmacies regularly to enforce compliance. To do this, state pharmacy boards must be provided with additional resources to adequately train and deploy surveyors to assess compliance.
>
> 2) FDA should work collaboratively with the state boards of pharmacy to provide them with the necessary support and training to survey compounding pharmacies for compliance with Chapter 797. Compounding pharmacies that distribute sizeable quantities (to be defined by FDA) of preparations, and those operating interstate, should be registered with FDA and subject to periodic inspections. ISMP also is encouraging the FDA to move forward with plans to publish

[14] Exhibit 5.
[15] Notably, John W. Culclasure, M.D. testified that he assumed a compounding pharmacy was FDA-regulated, and he "didn't know that a drug could be sold in the United States and not be FDA-approved." Deposition of John W. Culclasure, M.D. at 122:6-7, 123:9-14.
[16] *Id.*
[17] *See* Exhibits 6 & 7.

guidance documents on compounding practices and outline requirements for registration and inspection.

3) Pharmacies and pharmacists/technicians who compound sterile preparations, regardless of where they work, should know and comply with Chapter 797 to the fullest extent possible.[18]

ISMP stated that USP 797 is enforceable by the FDA, and "the agency has the authority to inspect pharmacies and enforce the standard in the interest of public health."[19] ISMP reiterated the fact that since the early 1990s, including the tenure of David Kessler, MD as Commissioner, the FDA was aware of "multiple problems" with compounded medications that resulted in recalls, patient injuries, and deaths. However, when ISMP contacted FDA, no one at the FDA could clearly articulate how the FDA regulates compounding pharmacies.[20]

F. Pre-Outbreak Regulatory Action Concerning NECC

a. 1999 Massachusetts Board of Pharmacy Complaint

On October 27, 1999, the Massachusetts Board of Pharmacy (MBP) wrote to NECC President Barry Cadden explaining that the MBP had received a complaint that Mr. Cadden and NECC provided a practitioner with blank prescriptions in violation of 247 CMR §§ 9.01(1), 9.01(13).[21] The MBP issued an informal reprimand to NECC.

b. April 2002 FDA Inspection

On April 4, 2002, the FDA received an investigation request pertaining to NECC.[22] From April 9 to 16, 2002, the FDA and the MBP conducted a joint investigation

[18] Exhibit 6.
[19] Exhibit 7.
[20] *Id.*
[21] Mass BOP-00959.
[22] NECC FDA 000006.

of NECC stemming from two MedWatch (the FDA's Safety Information and Adverse Event Reporting Program) adverse incident reports regarding NECC's compounded betamethasone.[23] The FDA's investigation revealed that NECC's betamethasone repository was improperly stored, by merely being covered with aluminum foil while sterility and endotoxin test results were pending, and that, therefore, the samples taken after completion of sterilization were not representative of the product that remained in the beaker for up to another week. Barry Cadden explained to the FDA investigator that he did not want to waste money on vials or transfilling the vials if the lot ended up failing testing.[24] The investigators explained to Mr. Cadden that this was not an acceptable process to maintain sterility. On the second day of the inspection, Mr. Cadden challenged the FDA's authority, refused to cooperate with the investigation, and directed the FDA to his lawyer.[25]

c. October 2002 – February 2003 Inspection

The FDA received another NECC investigation request on August 2, 2002, and the FDA and MBP conducted another investigation of NECC between October 2002 and February 2003 in response to three (3) MedWatch reports concerning preservative-free MPA, the product that in late 2012 would cause the outbreak of fungal meningitis.[26] Mr. Cadden offered no response to FDA questions concerning how NECC determined its beyond use dates, how long in advance of receipts of orders NECC compounds

[23] NECC FDA 000010, 000033.
[24] Mass BOP-00952.
[25] Mass BOP-00947-48.
[26] Mass BOP-00921.

products, and whether NECC compounded copies of commercially available FDA-approved products.[27]

On February 10, 2003, the FDA issued a Form 483 ("483") listing its observations during the inspection. The 483 noted that NECC's sterile drug products did not have adequate documentation to verify that they met minimum standards, including a lack of documentation or written policies concerning sterilization and cleaning. The 483 also noted that the FDA's sample results illustrated problems with both sterility and potency of NECC's injectable steroid suspensions (betamethasone repository and MPA).[28]

During the investigation, Mr. Cadden told FDA investigators that NECC compounded sterile products before prescriptions were received, and that NECC maintained a 30-day, bulk supply of product.[29] The FDA categorized NECC as a manufacturer, but despite the fact that NECC was acting as a manufacturer and fit the criteria of the 2002 CPG warranting intervention by the FDA, the FDA referred the matter to the MBP with the recommendation that NECC "be prohibited from manufacturing until they can demonstrate ability to make product reproducibly and dependably. If state is unwilling to take action, recommend firm be enjoined for GMP deficiencies."[30] GMPs, or Good Manufacturing Practices (also called Current Good Manufacturing Practices, or cGMPs), apply to drug manufacturers, but not to traditional compounding pharmacies. On February 7, 2003, the MBP issued a letter to Mr. Cadden requesting that he respond to the MBP's concerns because, based on information from

[27] NECC FDA-000077-79.
[28] Mass BOP-00912.
[29] Mass BOP-000935.
[30] Mass BOP-00915.

the FDA, his professional practices did not match with his prior representations.[31] The MBP filed a complaint against NECC on February 10, 2003.[32]

NECC responded to the FDA's February 10, 2003, 483 on February 26, 2003, discussing corrective measures undertaken by NECC to correct observations listed in the 483, most of which involved the implementation of new Standard Operating Procedures ("SOPs") meant to address the FDA's concerns.[33] In May 2003, NECC supplemented its response to the 483, noting that it had completed the implementation of its new SOPs and implemented an aseptic process validation protocol.[34] NECC's letter insisted, however, that NECC was not subject to and would not comply with the GMPs, claiming that NECC was not a manufacturer.[35] Notably, the FDA repeatedly classified NECC as a "Manufacturer of Human and Animal Drugs" throughout its 2002-2003 Establishment Inspection Report.[36]

d. February 2003 FDA and MBP Meeting

At a February 24, 2003 meeting between FDA and MBP officials, the agencies agreed that the state, not the FDA, was in the best position to gain compliance from or take regulatory action against NECC.[37] David Elder, the Compliance Branch Director of the FDA New England District concluded the meeting by emphasizing the "potential for serious public health consequences" if NECC's compounding practices relating to sterile products do not improve.[38] The FDA pointed out that as long as NECC operated within

[31] NECC FDA 000095-97.
[32] Mass BOP-00905-06.
[33] NECC FDA 000165.
[34] NECC FDA 000176.
[35] NECC FDA 000177.
[36] Mass BOP-00915-16.
[37] Mass BOP-00888.
[38] Mass BOP-00889.

the limits of pharmacy practice pursuant to FDA CPG § 460.200, the FDA policy would defer to state authority for regulatory oversight.[39] However, it was clear that NECC was *not*, in multiple respects, operating within the limits of appropriate pharmacy practice under the 2002 CPG. The sheer volume of recalled vials of betamethasone and MPA, as disclosed in the letters from the attorneys for NECC, the nationwide scope of NECC's distribution of those recalled products, as well as other factors, demonstrated once again that NECC was a manufacturer requiring close oversight by the FDA.

e. April 2004 MBP Complaint

On April 27, 2004, the MBP received a complaint against NECC alleging that an employee of NECC had informed the complainant's purchasing technician that although NECC requested a prescription to dispense the product, the name of an employee of the purchaser would suffice.[40]The same NECC employee also had stated that other clinics used nurses' names for prescriptions, and had assured the purchasing agent that this practice was legal.[41] On November 8, 2004, Mr. Cadden wrote to the MBP regarding NECC's use of a Prescription Order Form to solicit orders.[42] The MBP never informed NECC that NECC could not use the Prescription Order Form, thereby implicitly approving NECC's use of it.

On September 21, 2004, the MBP voted unanimously to issue three advisory letters to NECC regarding complaints received, to seek a reprimand, and to impose a three-year probationary status with periodic inspection of NECC.[43] On October 4, 2004,

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[39] Mass BOP-00889-90.
[40] Mass BOP-00687.
[41] *Id.*
[42] Exhibit No. 724 to the deposition of Samuel Penta.
[43] Mass BOP-00683.

the MBP offered a Consent Agreement to Mr. Cadden and NECC to resolve the complaints received.[44]On November 11, 2004, Paul Cirel, Esq., on behalf of Mr. Cadden and NECC, wrote to Susan Manning of the MBP refusing to agree to the terms of the MBP's Consent Agreement as written, and proposing a modification of the terms.[45] On November 23, 2004, the MBP unanimously voted to deny NECC's proposal to a modification of the Consent Agreement, and it voted to bring a formal complaint against NECC for dispensing medication without patient-specific prescriptions.[46]

f. 2006 Consent Agreement Resolving MBP Complaints

In January 2006, the MBP, NECC, and Mr. Cadden entered into a non-public Consent Agreement, not reported to any other state licensing board, resolving all previous complaints before the Massachusetts Board of Registration in Pharmacy.[47] The terms of the Agreement placed Mr. Cadden on probation for one (1) year, but stayed the probationary period under the condition that NECC and Mr. Cadden would furnish documentation of an inspection by Pharmacy Support, Inc. ("PSI"), which was selected by the Massachusetts Board of Registration in Pharmacy.[48] Dated January 30, 2006, PSI reported its initial assessment of NECC facilities and procedures, which identified "numerous significant gaps" in NECC's operations, and noted that NECC "needs to be upgraded and enhanced to be in substantial compliance with United States Pharmacopeia 795 or 797."[49]

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[44] Mass BOP-00661.
[45] Mass BOP-00648.
[46] Mass BOP-00645; *see also* Mass BOP-00688-89.
[47]Mass BOP-00413, 00415. Although the records do not expressly indicate this, presumably this is simply a revised version of the October 2004 Consent Agreement, as there are no new complaints in the MBP records between October 2004 and January 2006.
[48] Mass BOP-00415-16.
[49] Mass BOP-00579.

The initial report by PSI identified over thirty (30) areas of concern, problems, and observations from its inspection of NECC.[50] Many of these were serious and presented obvious potential to harm patients. PSI issued its final report on April 7, 2006, which stated that NECC "made significant improvements over the past several months" and demonstrated the ability to comply with state and federal regulations.[51]The final report noted that despite NECC's progress, NECC needed to address five (5) areas of concern "to be in substantial compliance."[52] The report also indicated that Mr. Cadden "has committed to these enhancements," and that PSI "is satisfied with the progress to date and is confident that the remaining issues will be resolved in a short period of time."[53] It is notable that as early as April 2006, after PSI was selected to evaluate NECC, administrators of the MBP knew that Ross Caputo, PSI's principal and one of the PSI personnel involved in the inspection of NECC, had been convicted of fraud and a violation of the Food, Drug, and Cosmetic Act arising from the sales of medical devices that blinded eighteen (18) people.[54] This knowledge should have cast doubt on the competence of PSI and the accuracy of its evaluations of NECC. However, after corresponding with Mr. Cadden about the five (5) remaining issues of concern for PSI, the MBP President wrote Mr. Cadden on June 2, 2006, informing Mr. Cadden that NECC had satisfied its terms and conditions of the 2006 Consent Agreement, but noted that Paragraphs 5(f) and (g) were still in effect.[55]

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[50] *Id.*
[51] Mass BOP-00605.
[52] The report does not elaborate on what NECC must be in "substantial compliance" with. Presumably this refers to federal and state regulations and USP guidelines.
[53] Mass BOP-00606.
[54] *See* Exhibit 3.
[55] Mass BOP-00568. Paragraph 5, sections (f) and (g) required NECC to update its SOPs biannually and to keep written reports of adverse events, respectively. Mass BOP-00572-73.

g. 2006 FDA Warning Letter to NECC

On December 4, 2006, the FDA issued a Warning Letter to Mr. Cadden and NECC arising from events independent of the recalls of betamethasone and MPA manufactured by NECC.[56] The letter explained the basis for the FDA's jurisdiction over compounded drugs, and recited that the FDA had elected to direct its enforcement resources against establishments that raise the type of concerns associated with drug manufacturing and entities whose compounding practices result in significant violations of the new drug, adulteration, or misbranding provisions of the FDCA — which described NECC, as the FDA was aware.[57] It also noted the FDA's current enforcement policy regarding pharmacy compounding, located at CPG § 460.200.[58]

The Warning Letter stated that NECC was compounding trypan blue ophthalmic products as well as 20% aminolevulinic acid solution, copies of commercially available drugs.[59] Although NECC clearly met the criteria calling for regulation by the FDA under CPG 460.200, the FDA advised NECC that it was abandoning its role to oversee NECC.[60] The letter also stated that the products were misbranded under 21 U.S.C. § 352(f)(1) because their labeling did not provide adequate instructions for use.[61] Curtailing the sale and distribution of misbranded products is an express duty of the FDA.

The warning letter alleged that NECC was advertising a compounded "Extra Strength Triple Anesthetic Cream," a "new drug" not approved by the FDA, and was

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[56] Mass BOP-00220-21.
[57] *Id.*
[58] Mass BOP-00221.
[59] *Id.*
[60] Mass BOP-00222.
[61] *Id.*

acting like a manufacturer by developing a standardized anesthetic drug product, and by giving physicians "courtesy prescriptions."[62]The FDA admitted that it knew of actions that were "not consistent with the traditional practice of pharmacy compounding, in which pharmacists extemporaneously compound reasonable quantities of drugs upon receipt of valid prescriptions from licensed practitioners to meet the unique medical needs of individual patients."[63]The FDA expressed concern about the "public health risk" associated with the compounding of "Extra Strength Triple Anesthetic Cream," citing at least two (2) non-fatal and two (2) fatal reactions to a compounded topical local anesthetic cream containing high doses of local anesthetics.[64] The FDA stated that the compounded anesthetic cream was misbranded because it failed to provide adequate instructions on the label and possibly because the label was false or misleading.[65]

Additionally, the letter noted a complaint alleging that NECC was repackaging an approved drug, Avastin, into syringes for a non-approved use. Therefore, NECC was distributing a "new drug" in violation of Section 505 of the FDCA, in addition to distributing a misbranded drug.[66]The FDA also indicated that it was aware that NECC had told physicians' offices that using a staff member's name would satisfy the patient-specific prescription requirement.[67] Despite this, the FDA inexplicably assured NECC that it would do nothing.[68] The letter concluded that failure to promptly correct these

[62] *Id.*
[63] *Id.*
[64] *Id.*
[65] Mass BOP-00222-23.
[66] Mass BOP-00223.
[67] Mass BOP-00224.
[68] *Id.*

issues could "result in additional regulatory action without further notice, including seizure or injunction[.]"[69]

It should be noted that official Warning Letters from the FDA are not common and are issued only for serious deficiencies. During the year ending June 30, 2014, the FDA issued only 69 Warning Letters to the entire pharmaceutical/biotechnology industry.[70]

NECC responded to the Warning Letter on January 5, 2007, noting that the Warning Letter was based on a 23 month old inspection, NECC had had no contact with the FDA since the inspection that ended in January 2005, and that NECC was advised by counsel that the average turnaround time for warning letters was 110 days, whereas this Warning Letter arrived 684 days post-inspection.[71]

NECC's response disputed the FDA's regulatory authority, claiming that it was only compounding drugs pursuant to valid prescriptions and that it was not compounding copies of FDA-approved commercially available drugs.[72] NECC also disputed the FDA's characterization of its repackaging of Avastin as "manufacturing," and it denied that it told physicians it would fill prescriptions written in the name of a staff member, stating that such a practice "contradicts all of our standard operating procedures."[73]

Incredibly, on October 31, 2008, over 21 months after NECC's reply of January 5, 2007, the FDA replied to NECC's response to the 2006 Warning Letter, merely by reasserting its position that compounded drugs are "new drugs" under the FDCA and

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[69] *Id.*
[70] Exhibit 8.
[71] NECC FDA 000254.
[72] NECC FDA 000255-56.
[73] NECC FDA 000259.

subject to FDA regulatory authority.[74] The FDA also explained its policy of enforcing its CPG 460.200 in Massachusetts.[75] The FDA's reply letter assured NECC that the FDA would do nothing to address NECC's manufacturing and distribution of anesthetic cream products, but stated that NECC's repackaging of Avastin violated Sections 505 and 502 of the FDCA.[76] The FDA's letter went on to state that failure to correct these issues could result in enforcement action, including seizure of NECC products or an injunction against NECC.[77]

It is noteworthy that in the interim between NECC's January 5, 2007 response to the FDA's Warning Letter and the FDA's October 31, 2008 reply, the FDA received multiple Adverse Event Reports concerning Avastin compounded by NECC.[78] In response to these reports, the FDA issued an Inspection Request on September 16, 2008.[79] Three (3) days later, the FDA recognized that they had not replied to NECC's response of January 5, 2007 and questioned how this would affect the Inspection Request.[80] Serial internal FDA correspondence over the next several weeks detailed that the FDA's failure to issue a reply to NECC's January 5, 2007 response was now preventing them from inspecting NECC.[81] After issuing the reply on October 21, 2008, the FDA did not perform the inspection as requested on September 18, 2008, or take *any* action in response to the Adverse Event Reports. In my opinion, this inaction by the FDA is inexplicably, egregiously negligent.

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[74] NECC FDA 000277-78.
[75] NECC FDA 000278.
[76] NECC FDA 000280.
[77] *Id.*
[78] NECC FDA 000260-276.
[79] FDA_E00439615.
[80] FDA_E00426111-113.
[81] FDA_E00426309-313, FDA_E00427627-427666.

h. FDA Awareness of Pre-2012 Patient Injuries from NECC Products

On April 1, 2008, Bruce Ota contacted Samia Nasr regarding a complaint received by the FDA New Orleans District Office.[82] A pain specialist, Dr. Matthew Wallace, who treated fibromyalgia patients in New Orleans with epidural injections of betamethasone manufactured by NECC, reported finding discolored vials of the product. He administered vials of the product that appeared normal, but his fibromyalgia patients started having flare-ups and worsening condition as a result. Samples of the product were collected and tested. Mr. Ota concluded the email by stating that "this appears to be a new drug [NECC] is compounding."[83] Despite this knowledge, the FDA refused to take action to regulate NECC as a manufacturer.

In October 2008, the FDA's Los Angeles District Office received a report of a patient vomiting and urinating blood after receiving phosphatidylcholine infusion therapy manufactured by NECC.[84] Joey Quitania of the FDA's Los Angeles District Office notified the FDA's New England District office about the report.[85] On October 17, 2008, Mutahar Shamsi forwarded the report to Bruce Ota, telling Mr. Ota "we need to make sure the investigator follows up on this."[86]Mr. Ota followed up with Mr. Quitania to request samples of the NECC products associated with the patients' injuries, but the investigation apparently stopped there.[87]The FDA failed to enjoin NECC despite the receipt of additional information indicating that they were a threat to the public health.

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[82] FDA_E00426108-109.
[83] *Id.*
[84] FDA_E00427627-629.
[85] *Id.*
[86] *Id.*
[87] *Id.*

On October 27, 2008, Bob Durkin in the FDA's Division of New Drugs and Labeling Compliance contacted the FDA's New England District Office regarding a Klebsiella pneumonia outbreak in New York linked to triamcinolone made by NECC.[88]On October 17, 2008 the New York City Department of Health and Mental Hygiene (NY DHMH) was made aware of at least five (5) and possibly up to 17 people who were exposed to Klebsiella pneumonia, three (3) of whom were hospitalized.[89] Mr. Durkin reported that the exposures likely occurred at a pain clinic when the patients were administered an intravenous version of triamcinolone made by NECC, which was shipped to the pain clinic in an envelope with a "patient-specific" prescription attached. The clinic drew multiple doses from the single patient-specific vial and used the same vial for several patients. Mr. Durkin asked the FDA's New England District Office to contact the NY DHMH to obtain more details about the NECC drug. On October 30, 2008, Mr. Durkin received additional information from the NYC DHMH, responded that he would "review shortly and report back," but again failed to take action against NECC.[90]

i. August 2011 MBP Certified Statement

On August 12, 2011, the MBP issued a Certified Statement of Registration regarding NECC's Massachusetts license.[91] This Certified Statement represented the MBP's current stance on its regulation of NECC and was available to the public upon inquiry. The Certified Statement provided that NECC was licensed in Massachusetts as a "Retail Drug Store Permit," and that "no discipline has been taken against this

[88] FDA_E00426100-104.
[89] *Id.*
[90] *Id.*
[91] Exhibit No. 713 to the deposition of Samuel Penta.

licensee."[92] In my opinion, this may have been strictly accurate, but was misleading in view of the foregoing serious, repeated problems with NECC. This Certified Statement remained in effect with the MBP until the fungal meningitis outbreak of 2012.

j. Colorado Cease and Desist Order

During an April 5, 2011 routine inspection of Sky Ridge Medical Center in Lone Tree, Colorado by the Colorado Board of Pharmacy, investigator Lisa A. Cornett collected records detailing the receipt of prescription drugs purchased from NECC without patient-specific prescriptions.[93] On April 15, 2011, the Colorado Board of Pharmacy issued an immediate "Cease and Desist Order" to NECC, explaining that NECC was only licensed to dispense and deliver patient-specific prescription drugs in Colorado.[94]The Order recited that on January 17 and March 24, 2011, NECC distributed stock compound prescription drugs in Colorado in violation of Colorado Rev. Stat. §§ 12-22-130(2), 802. The Colorado Board of Pharmacy then ordered NECC to cease and desist "in engaging in the unlawful distribution of prescription drugs in the State of Colorado[.]"[95]

The Cease and Desist Order, the initial report that led to the Cease and Desist Order, and the documents supporting the Cease and Desist Order were received by the FDA on May 10, 2011.[96] There is no evidence that the FDA took *any* regulatory action whatsoever in response.

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[92] *Id.*
[93] Mass BOP-00153.
[94] Mass BOP-00154-55.
[95] Mass BOP-000154.
[96] FDA_E00428909.

On July 16, 2012, Regina Barell, a Consumer Safety Officer with the FDA in Colorado, emailed Bruce Ota, Amber Wardwell, and Karen Archdeacon of the FDA, suggesting that they "get in touch with the Massachusetts Board of Pharmacy if you haven't already to inform them of [NECC's] activity and to see if there are any actions [the MBP] may wish to take" as a result of the Colorado Cease and Desist Order.[97] On July 17, 2012, Mr. Ota responded to Ms. Archdeacon, asserting that the FDA was "not doing anything with compounding pharmacies" at the time, but "CDER said last year that we may do something at the end of this year with compounding pharmacies."[98] Again, this was an inexplicable lapse, in view of the FDA's knowledge of NECC's serious violations of the FDCA and USP 797 that could subject patients to serious injury or death.

On July 17, 2012, Susan S. Martin of the Colorado Board of Pharmacy conducted a routine inspection of Delta County Memorial Hospital in Delta, Colorado, where she discovered an invoice from NECC.[99]She then determined that NECC was not a registered drug manufacturer with the FDA and confirmed that the Colorado Board of Pharmacy had previously issued a Cease and Desist Order to NECC in April 2011.[100] On July 20, 2012, Ms. Martin issued a Special Report concerning the matter, and James Coffey of the MBP received the Special Report on July 27, 2012.[101] Mr. Coffey informed the Colorado Board of Pharmacy that the MBP would "respond as soon as possible following a thorough review and analysis of the same."[102] The response from

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[97] FDA_E00428907.
[98] *Id.*
[99] Mass BOP-00043.
[100] *Id.*
[101] Mass BOP-00040.
[102] *Id.*

the Massachusetts Board of Registration in Pharmacy and the FDA was the same: neither regulatory agency did anything, which, in my opinion, was an egregious dereliction of their responsibilities.

IV. Opinions

a. Summary

In my opinion, the FDA and Massachusetts Board of Registration in Pharmacy failed to exercise proper regulatory authority over NECC and failed to take the objectively reasonable regulatory actions that would have prevented the fungal meningitis outbreak of 2012. The FDA and the Massachusetts Board of Registration in Pharmacy are both at fault, and in my opinion, were grossly negligent in their failure to carry out their statutory duties. I also disagree with many of the opinions attributed to David Kessler, MD.

b. FDA Compliance Policy Guide Section 460.200

NECC did not qualify for exemption from the new drug requirements under FDA CPG § 460.200 because they did not operate in accordance with 21 U.S.C. § 353a, which exempts only pharmacies engaged in "traditional compounding" of medications for patient-specific prescriptions from the FDA's new drug regulations. The FDA knew, nearly ten (10) years before the fungal meningitis outbreak of 2012, that NECC was engaged in the *manufacture* of medication without patient-specific prescriptions, compounding copies of FDA-approved commercially available medications, and distributing drugs that were misbranded and sometimes adulterated. NECC should have

been in the regulatory crosshairs of the FDA. NECC became a catastrophe, but the FDA had all of the information it needed, well in advance of September 2012, to stop it.

NECC's compounding practices fit the FDA's proscribed activities detailed in CPG § 460.200. FDA knew that NECC was operating as a manufacturer: NECC dispensed misbranded and adulterated drugs, dispensed drugs without patient-specific prescriptions, and sent drugs nationally. There was no justification to abandon regulation of NECC given the express terms of CPG § 460.200. FDA should have classified NECC as an unregistered manufacturer for a decade before the fungal meningitis outbreak. The MBP also knew that NECC dispensed drugs without patient-specific prescriptions, as evidenced by the MBP's implied approval of NECC's Prescription Order Form. The MBP failed to take appropriate action in response to that knowledge.

The notion that NECC was not "FDA regulated" is absurd. As explained throughout this report, the FDA asserted regulatory jurisdiction over NECC for at least ten (10) years before the fungal meningitis outbreak of 2012. The conscientiousness and competence of that regulation are another question, but there is no question that NECC was "FDA regulated."

The FDA was profoundly negligent in its failure to properly regulate NECC. The FDA had more than ample warning that NECC was an unregistered manufacturer that was endangering patients, but the Agency was simply negligent in failing to exercise its regulatory authority over NECC to assure the safety and efficacy of its products. The FDA's approach to its regulation of NECC demonstrates an appalling lack of concern for NECC's threat to the public health.

c. FDA's Flawed Priority Setting

During Dr. Kessler's tenure as FDA commissioner, I witnessed the beginning of the FDA's flawed selection of priorities and allocation of resources with regard to regulatory action. An excellent example is the diversion of staff and field personnel to the seizure of 15,000 gallons of orange juice because it was made from concentrate, but was labeled "fresh." In my opinion, the FDA under Dr. Kessler, and continuing after his departure, placed too low a priority on science and public health and too high a priority on making the news cycle. Between 2002 and late 2012, the FDA should have focused more attention on and allocated more resources to significant threats to the public health like the rapid growth of aggressive compounders in general, and NECC in particular. The failure of the FDA, despite many opportunities to take timely regulatory action against NECC, allowed the fungal meningitis outbreak to occur.

It is unfortunate that the deposition of the FDA has been foreclosed by the Court. FDA-registered proprietary drug manufacturers pay significant "user fees" to the FDA in conjunction with applications and inspections. Non-registered compounders do not. An unanswered question is whether the absence of fees generated from inspections of compounding pharmacies played any role in the FDA's dereliction of its duty to regulate compounders like NECC who were, in truth, manufacturing large volumes of drugs claimed to duplicate approved formulations.

d. NECC an Imminent Hazard to the Public Health

Under 21 C.F.R. § 2.5, the FDA had the authority to declare a product or practice an "imminent hazard to the public health" when the evidence is sufficient to show that the product or practice poses a significant threat of danger to health by creating a public

health situation (1) that should be corrected immediately to prevent injury and (2) that should not be permitted to continue while a hearing or other formal proceeding is being held. In my opinion, information known to the FDA no later than December of 2006 established that NECC was an imminent hazard to the public health under 21 C.F.R. § 2.5, and should have resulted in immediate action by the FDA, either immediately requiring registration as a manufacturer, and compliance with the duties of a FDA-registered manufacturer, or by moving to enjoin NECC's ability to operate. With a history of repeated violations of the FDCA, MBP regulations, and USP 797, the FDA should have declared NECC an imminent hazard to the public health, and should have closed NECC or forced suspension of its ability to manufacture and dispense drugs until that process could be carried out with a reasonable expectation of safety.

In addition, the FDA could have and should have taken action to educate and warn healthcare providers about the risks of compounded products. In 2003, the Director of Health Care and Public Health Issues for the United States General Accounting Office, Janet Heinrich, testified before the U.S. Senate Committee on Health, Education, Labor, and Pensions that the FDA was aware of 200 adverse incidents involving 71 compounded products since 1990, including three (3) deaths and 13 hospitalizations, resulting from injections of contaminated compounded medications in 2001. In my opinion, this information should have alerted the FDA to the threat to the public health caused by compounding pharmacies. The FDA should have taken action to warn healthcare providers of the public health concerns associated with pharmacy compounding in general, and the specific risks associated with companies like NECC that were serial violators. The FDA again failed to take necessary action.

e. Burden of Proof with Manufacturers

On April 16, 1992, Dr. Kessler stated that the "burden of proof rests with the manufacturer" to show that their silicone breast implants were safe. Similarly, the burden of proof was on NECC to demonstrate that the medications it manufactured were safe, effective, and met the GMPs applicable to registered manufacturers. However, NECC repeatedly failed to do so, and the FDA failed to impose that burden on NECC.

f. 2011 ISMP Publications

The April 2011 publications by the ISMP called upon the FDA to engage in greater oversight of compounding pharmacies. These articles should have convinced the FDA to re-set priorities and to take the appropriate regulatory action against NECC. The FDA failed to do anything with respect to NECC.

If the FDA had performed a reasonably competent investigation of NECC as late as March of 2012, at which time the Massachusetts Eye and Ear Clinic complained of a lack of efficacy of bulk supplies of ophthalmic anesthetics ("sub-potency"), the FDA would have found that NECC was producing adulterated and misbranded drugs; copies of commercially available FDA-approved medications; medications not proven safe and effective, medications in bulk, and without patient-specific prescriptions; and failing to adhere to GMPs and USP 797.

g. 2011 Colorado Cease and Desist Order

Upon receiving the Colorado Board of Pharmacy Cease and Desist Order in 2011, the FDA's New England District Office should have notified the FDA's main

compliance office at headquarters and insisted upon action against NECC because the company was clearly operating as a manufacturer under CPG § 460.200, was selling adulterated and misbranded products, and failing to require patient-specific prescriptions. The April 2011 Cease and Desist Order from Colorado reported directly to the FDA was—or should have been—a watershed event. This regulatory finding from Colorado demonstrated that NECC was still engaging in precisely the type of conduct not permitted by a traditional compounding pharmacy, and precisely the type of conduct that warranted regulation under the 2002 CPG. Objectively reasonable action by the FDA in response to the Colorado Board of Pharmacy Cease and Desist Order would have avoided the fungal meningitis outbreak of 2012 and prevented morbidity or mortality of more than 800 patients.

h. Patient-Specific Prescriptions

Patient-specific prescriptions do not themselves establish an FDA safeguard for patients; they serve essentially as a "marker" for a business that functions as a pharmacy as opposed to a manufacturer. Therefore, I attach little significance to patient-specific prescriptions for protecting the public health. With reference to the 2012 fungal meningitis outbreak, if patient-specific prescriptions had been written for MPA manufactured by NECC, and those patient-specific prescriptions were filled from one (1) or more of the three (3) contaminated batches, the results would not have been different for the individual patients. Instead, the significance of patient-specific prescriptions is that they are essentially a volume-based marker that enables regulators to distinguish between traditional compounding pharmacies and manufacturers, not as a safety-related signal to the healthcare providers receiving product. In my opinion, the presence

of a patient-specific prescription would not have affected the quality, potency, or sterility of the medications produced by NECC ultimately received by STOPNC.

i. Due Diligence of STOPNC

Over-the-counter drugs, prescription drugs, bulk pharmaceuticals, imaging and monitoring equipment, contrast agents, medical devices, and other health care products are adjuncts to the delivery of health care services by physicians, nurses, hospitals and ambulatory surgery centers. It is unreasonable to suggest that health care providers and health care facilities should investigate and inspect every facility that manufactures the products they use. Investigation of the manufacturer, inspection of the facilities, and the ultimate assurance of safety and/or efficacy of products are the responsibilities of the regulators—namely, the FDA and state boards of pharmacy.

It has been contended in this case that the FDA's 2006 Warning Letter should have warned any reasonable health care provider away from doing business with NECC. Obviously, that was not perceived as sufficient warning, given the sheer number, and the reputation, of many of the purchasers of product from NECC. In fact, one could argue that the contrary is true. It would have been reasonable and appropriate for STOPNC, Ms. Schamberg, Dr. Culclasure, and other potential customers of NECC to assume that the FDA had resolved all problems with NECC covered in the Warning Letter within five (5) years before STOPNC first purchased MPA from NECC in June of 2011. In my opinion, it was appropriate for STOPNC, Ms. Schamberg, and Dr. Culclasure to assume that if the problems had not been resolved, the FDA would not have permitted NECC to continue to operate in interstate commerce. It was also appropriate for STOPNC, Ms. Schamberg, and Dr. Culclasure to assume,

based on the MBP's August 12, 2011 Certified Statement, that NECC was in good standing with the MBP, given that no disciplinary action had been taken by the MBP against NECC.

The 2006 Warning Letter was available to the public. However, other internal FDA documents related to NECC were not readily available to the public. Even if available through a Freedom of Information Act ("FOIA") request, it would have required months to conduct a FOIA request for information the FDA had about NECC, and there is no guarantee that meaningful information would have been provided to the health care provider making the request. The purpose of making FDA documents available through FOIA requests has nothing to do with allowing potential customers to investigate drug makers. The system is not designed nor was it a standard of practice that reasonable health care providers make FOIA requests every time they consider a new vendor that may possibly be under FDA scrutiny. During my 35-plus years in or following the health care regulatory field, I have not heard that notion advanced until now.

NECC operated like a manufacturer at least from 2010 to 2012. No reasonable health care provider purchasing products from NECC should have been expected to think otherwise. The scope of NECC's facilities, its sales force, its sales technique, its marketing of products, and its overall operation were virtually indistinguishable from other drug manufacturers. It was not unreasonable for health care providers to consider NECC to be regulated no differently than any other drug manufacturer they dealt with. Reasonable health care providers would not be expected to consider NECC the

equivalent of the typical corner pharmacy, compounding individual medications for patients.

The representations made by NECC to customers about the quality of its manufacturing processes would have been reassuring to any potential customer, or even to a regulator. It was the regulators' job, not the customer's, to determine whether the facts supported NECC's representations. The regulators failed.

V. List of Cases

The following is a list of all other cases in which I have testified as an expert at trial or by deposition in the past four (4) years:

1. *Hanks v. Amgen USA Inc.*, 56-2009-00342748 (Ventura Super. Ct., filed April 20, 2009).

VI. Compensation

I am being compensated at the rate of $700/hour for my time on this case. I will also be reimbursed for all expenses associated with this engagement. My compensation is not contingent upon the outcome of the case.

Henry I. Miller, M.D.

January 14, 2016

Date